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THE BIOLOGICAL STANDARDIZATION OF INSULIN.

II. THE MORTALITY AND GLUCOSE-PROTECTIVE TEST IN RATS AS A METHOD FOR THE BIO-ASSAY OF INSULIN.

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Introduction.

It is generally admitted that the accurate standardization of any potent remedy such as insulin is of great importance (1) for the proper adjustment of dosage in its clinical use and (2) for quantitative work of a purely scientific character. The ideal standardization would, of course, be a chemical one, based on the chemical isolation of the active principle. All attempts in this direction have been unsuccessful up to the present time, and for this reason use must be made of a more empirical method, namely, the determination of the biological effect of the drug in animals.

The rabbit tests.—Very soon after the discovery of insulin a very fortunate observation by Banting, Best, Collip, Macleod, and Noble (1922) paved the way for a feasible method of bio-assay. These workers found that in rabbits having received a subcutaneous injection of insulin, the blood sugar soon begins to fall. If a sufficient dose has been given, characteristic symptoms appear, which are followed very often by the death of the animal, unless the insulin effect is removed by the administration of glucose. The blood sugar level at which the convulsions usually appear in fed animals is about 0.045 per cent, whereas in starved animals it may be considerably lower. The potency of insulin was therefore expressed in terms of so-called rabbit units, one unit being the amount of insulin which would lower the blood sugar of a normal rabbit weighing about 2 kilograms to the convulsive level (0.045 per cent) in four hours. Practical experience in the clinic then led to the adoption of a clinical unit (3 clinical units = 1 rabbit unit), as it was found that the physiological units were too large for certain cases, thus making it necessary to give fractional units. In the commercial production of insulin in America and Canada the assay has been carried out by two rabbit methods: namely, (1) by measuring the average fall of blood sugar during five hours following the injection of insulin and (2) by noting the incidence of convulsions in a series of animals injected with graded

doses. We are informed that the first technique is used by the Connaught Antitoxin Laboratories of the University of Toronto, and the second one by the Eli Lilly Co.

Macleod and Orr (1924) recently have described the first technique as follows: "Normal blood is removed from the ear vein of nine rabbits which have been starved for 24 hours and the blood sugar determined. No rabbit is used whose normal blood sugar is below 0.100 per cent or above 0.125 per cent. Into one of the rabbits is injected an amount expected to correspond to one physiological unit or three clinical units. Into a second is injected an amount about 50 per cent greater. The other seven rabbits are injected with amounts varying from slightly below one unit to slightly below one-half unit. At intervals of 1½, 3, and 5 hours after injection, blood is again removed and the sugar determined. The results are then calculated by means of the following formula:

$$\text{"Clinical units per cubic centimeter} = \frac{a}{b} \text{ times } \frac{w}{c} \text{ times } 1.5,$$

where a is the difference between the normal blood sugar and the average of the blood sugars at 1½, 3, and 5 hours after injection; b the difference between the normal blood sugar and 0.045; c the number of cubic centimeters of insulin injected; and w the weight of the rabbit in kilograms.

"The highest results which agree within 25 per cent of one another are averaged to give the assay. If four out of the nine results agree within the limits, the assay is reported. If not, the assay is repeated next day on nine other rabbits, the amounts of insulin injected being those which gave the high assays on the previous day. Sometimes a result is obtained which is much higher than the others. This is not included in the average, and if not repeated during the second or subsequent assays it is disregarded."

The second method, i. e., the assay based on the incidence of convulsions, is carried out as follows: Rabbits previously kept on a standard diet and weighing about 2 kilograms are starved for 18 hours and injected subcutaneously with graded doses of insulin. The smallest dose which produces convulsions within 2½ to 3 hours in the majority of the animals injected is considered a rabbit unit. We are advised that in commercial practice 300 to 500 rabbits are required to standardize a batch of unknown potency by this method. The rabbits showing convulsions receive glucose as an antidote. After a period of rest, the animals are used again for assay purposes.

It is unfortunate that the published evidence on which the reliability of these methods is based is rather meager as to details of actual assays of different batches, and yet only by a presentation of such information could a true estimate of the reliability of the methods be reached.

Perhaps the most detailed account of the use of the rabbit as a test animal is that of Clough, Allen, and Root (1923), who conclude that animals showing abnormally high or low blood sugar values should be rejected for testing purposes, that not more than two tests should be made upon the same rabbit during a week, and that the dosage should be proportional to bodyweight and so regulated that a fall of not more than 0.070 gram of blood sugar is produced. They consider that the incidence of convulsions is an unreliable criterion for calculating the potency, and point out a number of criticisms of the rabbit test. In a preliminary report, Blatherwick, Long, Bell, Maxwell, and Hill (1924) state that the dose of insulin per kilo body weight of rabbit which is required to produce convulsions varies directly with the body weight and not as the square. They also find that a low carbohydrate diet preceding the test lowers the resistance to insulin, and convulsions are more easily produced in rabbits which previously had one or more convulsions. For this reason, the animals are prepared for testing purposes by the administration of a dose producing convulsions some days before the animals are used for assay.

Criticisms of the rabbit tests.—The selection of the rabbit for the bio-assay of insulin is undoubtedly advantageous in one respect, as this species is very highly susceptible to insulin. However, it is very difficult for different laboratories to obtain a stock of animals of the same degree of sensitiveness (Macleod, 1924, Clough, Allen, and Root, 1923), as different breeds seem to show quantitative differences in response to one and the same preparation. Then, again, the rabbit is subject to a great variety of infections, such as coccidiosis, snuffles, etc., which may have a marked influence on the response to insulin. Coccidiosis, particularly, is a disturbing factor as the presence or absence of this very common infection can only be ascertained by necropsy.

The method based on the occurrence of convulsions requires a very large number of animals (300 to 500), as different rabbits differ considerably in their susceptibility to convulsions, if injected with a threshold dose of insulin. The real cause of the convulsions, and the mechanism responsible for their occurrence are still incompletely understood (Macleod, 1924). We believe, however, that the convulsive method yields fairly accurate results, provided that the test is based on a very large number of animals.

The blood-sugar method assumes that the four sugar estimations before and after injection of insulin yield a quantitative estimate of the action of insulin on metabolism. This is far from the truth, as this view could only be accepted on the basis of a complete understanding of the action of insulin, and particularly the relation between the various changes produced by insulin in the anabolic and catabolic

phases of carbohydrate, protein, and fat metabolism, on the one hand, and their effect on the blood-sugar level on the other. Furthermore, it occurs sometimes that the maximum fall of blood sugar is considerably delayed; such abnormal results would, however, be eliminated by the use of a considerable number of animals for each test. Attention is also called to the fact that the fall in blood sugar is not directly proportional to the dose of insulin, but assumes a logarithmic relation, at least in the case of the depancreatized dog (Allan, 1924).

Attempts to improve existing methods.—A proper appreciation of these various defects of the rabbit methods has led to attempts to improve the existing methods. Thus, Eadie and Macleod (1923) studied the feasibility of using the antagonistic action of epinephrine on the hypoglycemic effect produced by insulin for purposes of assay of the latter. According to Macleod (1924) this method had to be abandoned. On theoretical grounds the use of epinephrine would introduce merely another variable factor, i. e., variation in the response of different animals to epinephrine.

Ringer (1923) suggested the use of phloridzinised animals for purposes of assay. As far as we can judge, this method has failed to yield accurate results, and it is also open to criticism as introducing another variable factor.

Theoretically, the most accurate assay should be obtained by the determination of the glucose equivalent, i. e., the extra amount of sugar metabolized in a completely depancreatized animal after the injection of insulin. Complete removal of the pancreas would eliminate one possible variable factor, namely, variations in the liberation of insulin from the pancreas. Allan (1924) has recently tested the feasibility of this idea, but his interesting results would hardly permit a final conclusion. Moreover, work with completely depancreatized dogs requires considerable technical ability and it would be difficult to keep such animals in exactly the same nutritional state for considerable periods of time.

Attempts were made also to use mice instead of rabbits. Mice are rather sensitive to insulin. When kept at 28° C., Krogh (quoted by Macleod, 1924) has found that they develop characteristic symptoms; whereas at a lower atmospheric temperature the resistance is considerably greater. Krogh and Dale (personal communication) have worked with mice, using as a criterion of the potency of insulin the minimum dose which produces characteristic symptoms in a certain percentage of the animals. Fraser (1923) has also used mice and has obtained encouraging results, although his method has not yet been accepted by the Toronto Insulin Committee.

At a recent conference on the biological standardization of drugs held in Edinburgh in July, 1923, under the auspices of the Health Committee of the League of Nations and attended by the senior

author of the present report, the question of the bio-assay of insulin was considered. Reports were made by Macleod and Krogh, and after discussion the conference adopted the following resolution:

> That the conference recommend that, for the present, one unit of insulin be defined as one-third of the quantity which lowers the blood sugar to the convulsant level of 0.045 per cent, in a normal rabbit of approximately 2 kilogram body weight which has been starved for a period of 24 hours prior to the injection.

The conference agreed that the present method should be improved or substitutes discovered, and suggested that the dextrose equivalent in the completely depancreatized dog may be more suitable. It was also decided to accept the offer of Professor Dale for the preparation and distribution of a dry, stable sample of insulin for use as a standard for comparison. This standard preparation should serve to eliminate variations due to seasonal and local variations in the resistance of animals.

Experimental.

About a year ago we began work on this subject with a view of testing out the value of standardized rats for the bio-assay of insulin. Extensive experience in this laboratory with the standardization of arsenicals by means of albino rats suggested the possibility that this species might serve equally well for the standardization of insulin. For obvious reasons it would be easier to work with animals smaller than the rabbit. Preliminary work dealt with the preparation of insulin and the study of its action when injected by different routes into rats kept as far as possible under standard conditions. In a preliminary paper (Voegtlin and Dunn, 1923) it was pointed out that rats treated with insulin develop gradually increasing weakness which ultimately passes over into coma, the respiration becoming very shallow. Profuse salivation is noted and a small proportion of the animals develop convulsions, similar in nature to those observed in rabbits. If the dose is sufficiently large, the rats die of respiratory failure and autopsy reveals pulmonary edema and no other gross changes. With sublethal doses the animals begin to recover in the course of the first two hours and are often practically restored in 3, 4, or 5 hours. The day following the injection, the animals appear practically normal, though they may have had very severe symptoms. Late deaths, such as have been described in rabbits treated with insulin, have never occurred in rats, though we have used many thousands of animals.

The preliminary tests showed that rats require a larger dose of insulin per kilogram body weight for the production of symptoms than do rabbits. The rat is, therefore, more resistant to insulin.

It is obvious that the animals used for standardization purposes should be standardized as far as possible.

Strain.—In order to eliminate difference in response due to difference in the strain of rats only one standard strain was used. This was obtained from a rat breeder. The rats when received weigh about 60 grams and are free from disease. The males are separated from the females so as to eliminate pregnancy.

Diet.—In order to adjust the metabolism, the animals are put on a standard diet of the following composition:

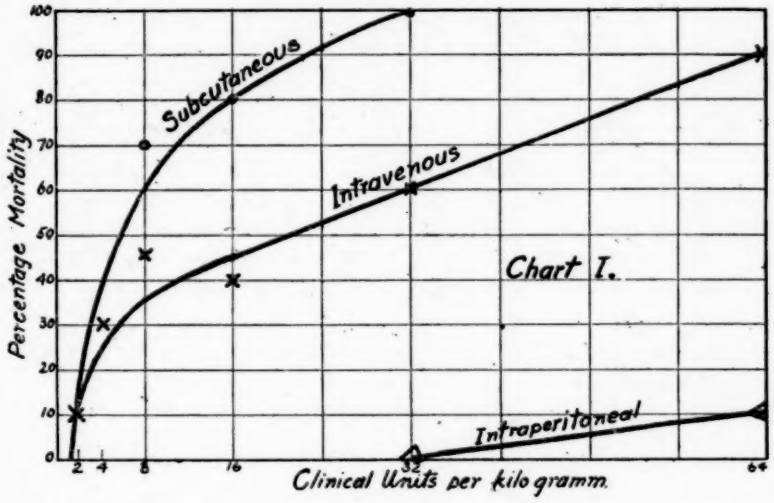
Graham flour	16 lbs.
Milk powder	10 lbs.
Corn meal	3 lbs.
Cod liver oil	300 c. c.
Sodium chloride	150 gms.
Calcium carbonate	10 gms.

These ingredients are mixed thoroughly and enough water is added to form a dough. Cakes of convenient size are then made and dried over metal screens at ordinary room temperature. The finished cakes are fairly hard and economical in use. The increase in body weight of young rats kept on these cakes and a liberal supply of fresh water indicates that the diet insures a normal rate of growth and perfect health. As soon as the animals have reached 110–130 grams they are ready for assay purposes. At about 3 o'clock in the afternoon preceding a test a sufficient number of rats are put into wire screen cages and placed in an incubator room at 28°–30° C. for 18 hours. This is done in order to eliminate the influence of variations of atmospheric temperature on the susceptibility of rats to insulin (Voegtlin and Dunn, 1923).

Incubator room.—The incubator room is constructed of white pine or any other high-grade wood, with inside dimension 41.5 by 50 by 85 inches, giving about 100 cubic feet of air space. Five 14-inch wooden shelves are placed at the side opposite a door with glass windows, which allows an unobstructed view of the interior without unnecessary opening of the incubator. The heating units consist of eight 40-watt mazda electric light bulbs, set in parallel, four on either side near the floor. These are inclosed in sheet metal boxes 6 by 11 by 19 inches to deaden the intensive illumination. The boxes have no bottoms, and the tops have numerous 1-inch perforations to permit free heat radiation. A de Khotinsky bimetallic thermo-regulator is set into line from the lighting circuit, and adjusted to control the temperature at about 29° C. An excess of lights is used in order that the temperature may be quickly raised to the maximum after entering the room for the purpose of examination of the animals. To insure free circulation of air in the incubator, a 3-inch opening is made in the roof, and a series of 1-inch openings is cut in the bottom of the door. A small electric fan is placed on the floor and directed upward so as to give a free circulation of air. Loss of humidity is overcome by placing a large beaker of water on the top of one of the lamp boxes. A graphic thermo-recorder placed inside the incubator has indicated

that this simple construction insures a satisfactory control of temperature. An incubator of this size will easily accommodate twenty to thirty cages containing five rats each or a total of 100 to 150 animals. The initial expense of construction and the cost of operation of the incubator are very small.

Method of injection.—While the rats are in the incubator room all food and water are withdrawn. On the following morning the rats are weighed and marked by the use of a skin stain. They are immediately injected subcutaneously with insulin (concentration adjusted so as not to exceed 1 c. c. per dose) and replaced at once in the incubator. We have found that the subcutaneous, intraperitoneal, and intravenous administration of insulin produce the same



symptoms in rats; the dose necessary to produce symptoms or death varies, however, with the mode of injection (Chart I).

It will be seen that the subcutaneous injection produces the greatest effect, the intravenous injection being slightly less effective, and the intraperitoneal mode of administration being the least effective.[1]

We finally have adopted the subcutaneous method for the following reasons: First, this is the method used clinically; second, the presence of any toxic impurities, such as albumoses, histamine, etc., would not increase the toxicity of the preparation as much as when given intravenously; and third, the subcutaneous injection insures a more gradual absorption, slower rate of elimination and, therefore, more

[1] The low effectiveness of the intraperitoneal injection may possibly be due to the ability of the liver to dispose of a large part of injected insulin in some unknown way, thus preventing access of the drug to the general circulation.

prolonged effect, than when the insulin is injected directly into the circulation. Technically, subcutaneous injections also require much less time than the intravenous injections, and the latter method does not increase the accuracy of the results.

TABLE 1.—*Blood sugar of normal albino rats on standard diet starved 17 hours previous to bleeding.*

Rat No.	Weight.	Blood sugar.	Rat No.	Weight	Blood sugar.
	Gms.	*Per cent.*		*Gms.*	*Per cent.*
1	124	0.113	44	118	0.108
2	100	.116	45	114	.106
3	100	.107	46	122	.116
4	104	.121	47	124	.114
5	100	.126	48	130	.109
6	130	.119	49	114	.103
7	110	.115	50	120	.107
8	130	.115	51	118	.108
9	114	.112	52	128	.101
10	104	.117	53	124	.108
11	102	.116	54	124	.108
12	130	.107	55	114	.107
13	120	.113	56	122	.109
14	104	.119	57	118	.103
15	102	.135	58	122	.111
16	128	.103	59	116	.100
17	104	.110	60	112	.109
18	122	.121	61	112	.103
19	114	.107	62	116	.111
20	128	.108	63	121	.115
21	112	.107	64	113	.108
22	106	.117	65	113	.105
23	106	.118	66	126	.102
24	118	.115	67	125	.101
25	104	.122	68	125	.108
26	102	.117	69	115	.113
27	102	.114	70	125	.107
28	104	.113	71	118	.107
29	112	.114	72	116	.119
30	102	.109	73	121	.108
31	112	.115	74	102	.113
32	104	.116	75	110	.117
33	110	.113	76	130	.130
34	114	.113	77	118	.114
35	100	.111	78	118	.127
36	102	.113	79	118	.109
37	108	.106	80	130	.143
38	116	.111	81	118	.148
39	104	.108	82	108	.144
40	104	.108	83	100	.123
41	120	.107	84	108	.130
42	114	.106	85	104	.128
43	110	.106			

Average weight=114 gms. All males.
Average per cent of blood sugar=0.113.

Blood sugar as affected by starvation and insulin.—It was desirable to determine the blood sugar in rats after the period of starvation and also following the injection of insulin. The variation of the blood sugar of starved rats, as affected by age, season, and sex will be the subject of a separate report. Suffice it to say here that the usual variations are observed in rats as are noted in rabbits. Table 1 gives the blood sugar values of standard male albino rats starved for 17 hours previous to bleeding. The blood was obtained by decapitation of the animal and collection of the blood in small glass vials containing a film of dry potassium oxalate. Myers and Bailey's modification (1919) of the Lewis and Benedict method was used,

employing 1 c. c. of blood. It will be seen from Table 1 that the average percentage of blood sugar is 0.113 gram, with a minimum of 0.100 gram and a maximum of 0.148 gram. This represents the physiological variation under standard conditions. Table 2 shows that 42 hours of starvation does not materially change the values obtained with a period of starvation of 17 hours. Chart II shows the frequency curve of the blood sugar values of rats. It will be noted that the curve is much steeper than that obtained with rabbit blood (Scott and Ford, 1923).

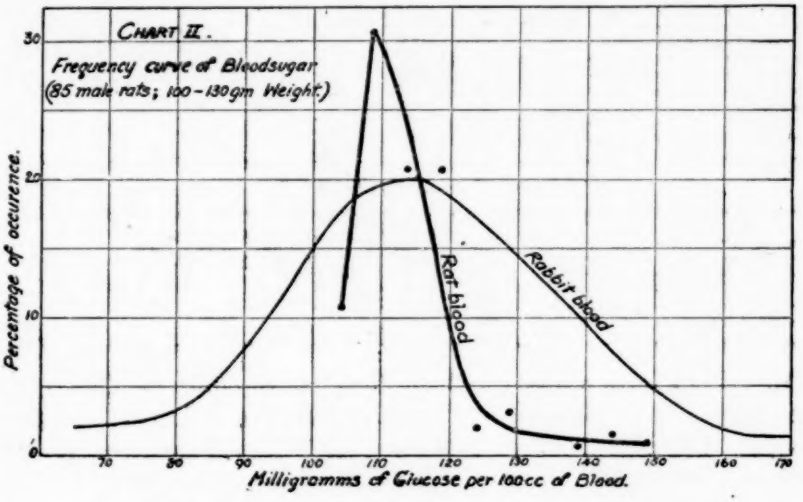


TABLE 2.—*Normal blood sugar of male rats starved 42 hours.*

Rat No.	Weight.	Blood sugar.	Rat No.	Weight.	Blood sugar.
	Grams.	*Per cent.*		*Grams.*	*Per cent.*
1	104	0.111	6	108	.102
2	120	.110	7	118	.111
3	108	.122	8	108	.112
4	110	.112	9	104	.121
5	108	.111	10	112	.122

TABLE 3.—*Blood sugar and symptoms of normal female rats after subcutaneous injection of insulin.*

INSULIN PREPARATION NO. 1.

Rat No.	Time after injection.	Blood sugar.	Symptoms.
	Minutes.	*Per cent.*	
1	93	0.049	
2	108	.053	
3	141	.051	Killed on appearance of convulsions.
4	171	.050	
5	103	.052	
6	121	.053	
7	87	.052	
8	117	.049	
9	54	.052	
10	106	.052	

TABLE 3.—*Blood sugar and symptoms of normal female rats after subcutaneous injection of insulin*—Continued.

INSULIN PREPARATION NO. 2.

Rat No.	Time after injection.	Blood sugar.	Symptoms.
	Minutes.	*Per cent.*	
11	62	0.049	
12	31	.060	
13	31	.046	
14	60	.049	
15	26	.048	
16	30	.055	Killed on appearance of convulsions.
17	37	.055	
18	79	.043	
19	32	.054	
20	28	.043	
21	53	.054	
22	77	.046	
23	62	.054	
24	128	.046	

INSULIN PREPARATION NO. 3.

25	160	0.068	Depression; slight paralysis.
26	120	.059	Paralysis; mild convulsions.
27	180	.063	Slight paralysis.
28	240	.090	Do.
29	60	.063	Do.
30	120	.054	Do.

In Table 3 data are given which illustrate the drop of blood sugar resulting from the injection of insulin, using the technique described above. The animals were killed when symptoms of various degrees of intensity appeared. It will be noted that the appearance of severe symptoms (convulsions or coma) is associated with a marked fall of blood sugar to about 0.050 from an average of 0.113 before injection. Milder symptoms (depression and slight paralysis) are accompanied by a smaller fall in blood sugar (rat 25, blood sugar 0.068). A number of blood sugar estimations of animals having recovered from the convulsions or coma and made 24 or 48 hours after the injection with insulin and continued withdrawal of food showed that the blood sugar had returned to the normal starvation level (Table 4). This fact indicates that sufficient glucose is mobilized from the glycogen stores or formed from protein and fat to compensate for the previous loss of blood sugar. In view of the fact that the figures for the glycogen content of muscle and liver (given below) show that the glycogen stores are very low before and after the administration of insulin to starved rats, it is suggested that the return of the blood sugar to normal 24 hours after administration of insulin is brought about to a considerable extent by the formation of glusose from protein and fat. This view is in harmony with some recent observations of Osborne and Mendel (1924) which prove that sufficient glucose is formed on a diet entirely lacking in carbohydrates to keep rats in good health and permit normal growth.

TABLE 4.—*Blood sugar and symptoms of normal albino female rats 24 and 48 hours after injection of insulin.*

INSULIN PREPARATION NO. 2.

Rat No.	Time after injection.	Blood sugar.	Symptoms on day of injection.
	Hrs. min.	*Per cent.*	
31	47 25	0.100	Depression; paralysis; recovery.
32	47 16	.090	Beginning paralysis; convulsions; recovery.
33	47 44	.130	Depression; slight paralysis; convulsions; recovery.
34	47 54	.110	Depression; paralysis; convulsions; recovery.
35	47 34	.112	Depression; paralysis; recovery.
36	47 38	.102	Depression; paralysis; convulsions; recovery.
37	47 57	.124	Paralysis; convulsions; recovery.
38	24	.112	Depression; paralysis; recovery.

Glycogen content of skeletal muscle and liver.—Information as regards the glycogen content of the skeletal muscle and liver of rats before and after injection of insulin is of interest in connection with the action of the drug in this species. The method of Pflüger (see Plimmer: Practical Organic and Bio-chemistry, p. 209) was used for the determination of glycogen. The glycogen so obtained was hydrolyzed in the usual manner and the resulting glucose titrated by Bertrand's method.

TABLE 5.—*Glycogen content of normal male albino rats starved 17 hours in constant temperature closet. Chloroformed.*

Rat No.	Body weight.	Weight of liver.	Glycogen.	
			Liver.	Muscle.
	Grams.	*Grams.*	*Per cent.*	*Per cent.*
1	106	4.20	0.027	0.072
2	100	5.00	.009	.081
3	102	6.50	.018	.126
4	100	5.15	.018	.072
5	94	5.70	.018	.081
6	100	5.52	.009	.081
7	102	5.55	.018	.112
8	102	5.15	.009	.090
9	100	5.80	.009	.090
10	104	4.82	.018	.063
Average	100	5.33	.018	.090

TABLE 6.—*Glycogen content of normal albino rats starved 17 hours in constant temperature closet. Bled to death.*

Rat No.	Body weight.	Sex.	Weight of liver.	Glycogen.	
				Liver.	Muscle.
	Grams.		*Grams.*	*Per cent.*	*Per cent.*
1	96	♀	3.30	0.027	----------
2	94	♂	3.60	.063	0.045
3	92	♂	3.45	.108	.117
4	96	♂	3.50	.036	.045
5	98	♂	3.65	.045	.126
6	94	♂	3.45	.045	.126
7	94	♂	3.40	.045	.090
Average	95		3.48	.053	.092

Tables 5 and 6 give the glycogen content of the liver and skeletal muscles of rats starved for 17 hours. It will be noted that the average percentage glycogen content of the liver is 0.018 if the animals are killed by chloroform and 0.053 if the animals are bled to death. The difference in these figures is due to the fact that death from chloroform leaves a very large amount of blood in the liver (compare liver weight of the two series), thus reducing the glycogen percentage of the organ. The glycogen content of the skeletal muscle, on the other hand, shows an average of 0.090 and 0.092 per cent, respectively—practically no difference. This organ is not so vascular as the liver and therefore differences in the method of killing the animal do not have the same influence on the estimated glycogen as in the case of the liver. Table 7 shows that insulin given in doses sufficient to produce coma or convulsions is accompanied by a fall of 49 per cent of liver glycogen and 60 per cent of muscle glycogen. Attention is called to the fact that all glycogen figures are very low, this being due to the fairly long period of preliminary starvation.

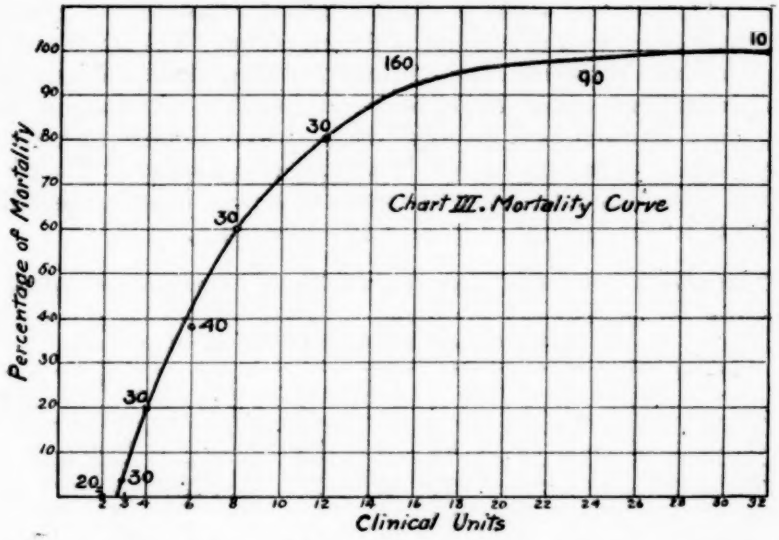
TABLE 7.—*Glycogen content of albino rats after injection of insulin; rats starved 17 hours in constant temperature closet before injection. Bled to death.*

Rat No.	Body weight.	Sex.	Weight of liver.	Glycogen (per cent).		Symptoms.
				Liver.	Muscle.	
	Grams.		*Grams.*			
1	102	♂	4.30	0.036	0.027	Slight paralysis; paralysis, died.
2	100	♂	4.20	.036	.027	Slight paralysis; died.
3	98	♂	4.60	.036	.045	Paralysis; died.
4	100	♂	4.60	.027	----------	Do.
5	98	♂	4.70	.027	----------	Do.
6	102	♀	3.25	.027	.036	Convulsions; died.
7	104	♂	4.60	.027	.054	Slight paralysis; died.
8	102	♂	5.00	.036	.054	Do.
9	100	♂	4.25	.036	.027	Do.
10	102	♀	4.20	.027	.045	Do.
11	102	♂	5.10	.018	.027	Slight paralysis; paralysis; died.
12	102	♀	4.90	.018	.027	Paralysis; died.
13	100	♀	4.90	.018	.036	Slight paralysis; paralysis; died.
Average	100	------	4.51	.027	.036	

Individual variation in susceptibility.—As in other animals, so also in rats, there is a striking individual variation in the susceptibility to the action of insulin. In spite of all possible precautions aiming at the elimination of factors which might operate in this direction (diet, atmospheric temperature, breed [1]), it is impossible to eliminate individual variations in susceptibility. The criteria used were (1) the absence or the intensity of symptoms in a series of standardized rats, and (2) the mortality rate. Data illustrating the former will be presented later. In Chart III a mortality curve is given, obtained by noting the percentage of deaths occurring in a series of 440 rats with an average body weight of approximately 110 grams and in-

[1] Sex seems to have no influence on the toxicity.

jected with increasing doses of the same lot number of insulin. The percentage mortality on each dose is plotted as ordinates and the dose, expressed in clinical units per kilo body weight, as abscissae. The figures on the curve indicate the number of animals injected with each dose. This curve is typical for a large number of other curves obtained with other lots. It will be noted that no death occurs with 2 clinical units. Three units give a mortality of 4 per cent; and from there on the curve proceeds in regular fashion up to 16 units, which shows a mortality of 95 per cent. Beyond this point the curve flattens out and the results remain between 90 and 100 per cent. The explanation of this curve is obviously as follows: The fatal threshold dose lies between 2 and 3 units; below this no animals will die; above this limit the more susceptible animals will die in increasing numbers as the dose is increased. The flattening out of the curve



above 16 units is due to the fact that there are always a few of the animals (5 to 10 per cent) which are highly resistant to the action of insulin. The results of the toxic action of insulin are, therefore, not unlike those obtained with arsphenamine.

Mortality test or M. L. D.—If the mortality test is to be used as a criterion of the potency of insulin preparations, the definition of the minimum lethal dose is a matter of convention. At one time we considered the M. L. D. the dose which would kill 45 to 55 per cent of the animals injected. This definition has much in its favor; but for reasons which will become apparent later on, we have decided to consider the *M. L. D. the smallest dose which will cause a mortality of 90 to 100 per cent* when standardized rats are injected subcutaneously with increasing doses varying 100 per cent in strength, not less than 10 animals being used for each dose. It is perfectly feasible

to reach a fair estimation of the potency of insulin preparations by means of the mortality test, especially if the test is repeated and the M. L. D. is obtained by means of a curve constructed in the manner described above. Some of the results obtained by the application of this technique to a fairly large number of commercial preparations of insulin are given in Table 8. The commercial preparations were obtained through the courtesy of the Connaught Antitoxin Laboratories of the University of Toronto and Eli Lilly & Co., Indianapolis, Ind. These commercial lots were passed by the Insulin Committee of the University of Toronto as complying with the standards set up by this committee and the date of release of these preparations is between October 15, 1923, and April 15, 1924. In addition to these preparations a few lots were purchased in the open market. Each lot was tested as soon as possible, the test being repeated in the case of some lots several weeks or months later for the purpose of ascertaining the presence or absence of deterioration. The ampules were kept in their original containers protected from light and excessive fluctuations of atmospheric temperature. The commercial lots contained tricresol as a preservative, and were diluted with sterile physiological saline so as to obtain a 20 per cent solution. The pH of this solution was determined by means of indicators and gave values of 5.2 to 5.8 for brand B and 3.6 to 5.8 for brand A.

TABLE 8.—*Mortality tests (percentage mortality) on commercial preparations.*

Lot No.	Dose in clinical units (as stated on label) per kilo body weight.									
	2	3	4	6	8	12	16	24	32	48
1		0	30	40	50	80	*100	100		
2			0	10	50	50	70	80	*100	
3			0	0	30	75	*100			
4			0	20	25	70	*90	100		
5				0	10	70	*90	90	100	
6					0	0	20	30	60	60
7				20		70		*100		
8				*90		100		100		
9				25		*95		100		
10	0			15	45	*90	90			
11			0	20	55	80	*90	100	100	
12		0	17	46	67	83	*98			
13	0	0	7	10	33	55	80	85		
14				40		*100		100		
15				40		*100		100		
16	0	0	13		73	*100	95			
17				20		80		*95		
18			10		65		*95			
19	0	3	20	38	60	80	*95	91	100	

* M. L. D.

The data presented in Table 8 illustrate some of the findings of the mortality test carried out on commercial preparations. Attention is called to the fact that there are considerable variations in the M. L. D. of insulin Nos. 1 to 9, the M. L. D. of the most potent preparation (No. 8) being 6 units per kilogram body weight, whereas 48

units of No. 6 caused a mortality of only 60 per cent. Larger doses of this preparation could not be given as the supply of this lot was exhausted. It is impossible to decide whether this low value was due to deterioration or whether the original standardization on rabbits had been faulty. Taken as a whole, the average M. L. D. of these preparations falls quite close to 16 units. Lots 10 to 19, representing another brand of insulin, show less variation, the average M. L. D., with the exception of lot 17, being either 12 or 16 units per kilo. The supply of lot 17 was not sufficient to permit of carrying out more tests, but it is quite likely that 16 units may represent the actual M. L. D. of this lot.

In order to obtain further evidence as to the reliability of the mortality test, certain lots of insulin were treated with adsorbing agents (fuller's earth, charcoal). The mortality test showed that the potency was completely lost as a result of removal of the active principle by the adsorbing agents. Treatment of insulin solution with sodium hydroxide also revealed destruction of the active principle as shown by the mortality test. These observations agree with similar observations made by others where rabbits were used. The outcome of these experiments, therefore, adds strength to the assumption that the mortality test actually determines the potency of insulin.

As of further interest in this connection we present a few protocols on the prompt relief of the symptoms produced by insulin in rats following intravenous injections of *small* amounts of glucose. The glucose was administered as soon as severe symptoms (convulsions or coma) appeared.

Rat 1: Convulsions; 1 minute after 0.063 gm. glucose per kilo showed marked improvement. This was followed by relapse, but the animal survived.

Rat 2: Convulsions; greatly improved 1 minute after 0.063 gm. glucose per kilo, but died during following night.

Rat 3: Coma; walked about 1 minute after 0.063 gm. glucose, but died 35 minutes later.

Rat 4: Convulsions; walked about 1½ minutes after 0.125 gm. glucose per kilo. Survived.

Rat 5: Coma; walked about 1 minute after 0.125 gm. glucose per kilo. Had relapse, but survived.

Rat 6: Convulsions; walked about 1 minute after 0.125 gm. glucose per kilo. Had relapse, but survived.

Rat 7: Coma; recovered 2 minutes after 0.125 gm. glucose per kilo. Had relapse, and died 84 minutes after glucose injection.

Rat. 8: Convulsions; walked about 30 seconds after 0.25 gm. glucose per kilo. Had relapse, and died 56 minutes after glucose injection.

These results plainly indicate that very small amounts of glucose promptly remove the hypoglycemic symptoms. The symptoms are therefore entirely due to a deficiency of glucose.

Glucose protective test.—It might be argued, however, that the results obtained by means of the mortality test are complicated by the presence in the preparation of toxic substances (histamine, albumoses, peptones), and that at least part of the toxic action is due to these impurities. Moreover, the mortality test might be criticized as using an end point far removed from the usual conditions prevailing in clinical cases, with exception of cases of diabetic coma. In order to meet this criticism we developed the so-called glucose protective test. This test is based on the well-established fact that glucose is a physiological antidote for insulin. If it were possible to express the potency of a given preparation in terms of the amount of glucose (glucose equivalent) required to protect rats injected with a M. L. D., the figures so obtained would be of great value. The procedure as finally adopted is as follows: A series of 50 rats is injected subcutaneously, as described, with the M. L. D. of insulin. Ten rats are kept as controls, the other 40 animals receive, in groups of 10 each, immediately after the insulin injection, a 20 or 40 per cent solution of pure glucose in water by stomach tube in the following doses:

10 rats, 1 M. L. D. insulin	Controls.
10 rats, 1 M. L. D. insulin	+5 grams per kilo glucose
10 rats, 1 M. L. D. insulin	+6 grams per kilo glucose.
10 rats, 1 M. L. D. insulin	+8 grams per kilo glucose.
10 rats, 1 M. L. D. insulin	+10 grams per kilo glucose.

The rat receiving the glucose solution is held by an assistant, and a so-called Zebra French catheter of size 7 is easily introduced into the stomach. The catheter is connected with a graduated syringe, both catheter and syringe having been filled with the glucose solution before insertion of the catheter into the stomach. The calculated amount of solution is then introduced, the catheter is withdrawn, and the animal is placed in the incubator room. With a little practice this operation is done very easily and requires no more time than any other injection.

The results obtained with the glucose protective test have been very gratifying. Table 9 shows the variations in the results which may be expected. The data in this table were obtained by repeating the test on one large standard lot of insulin obtained through the courtesy of Eli Lilly & Co. The results indicate plainly that the test is quite accurate. With one exception the variation did not exceed 20 per cent, i. e., the protective dose of glucose was between 8 and 10 grams per kilo body weight.

TABLE 9.—*Glucose protective test of standard insulin.*

Dose of insulin=16 clinical units per kilogram. Glucose given as 40 per cent solution. Number of animals injected with each dose=10.

Date of test.	Glucose.	Mortality.	Time of death after injection (average).	Symptoms.
	Gms. per kilo.	*Per cent.*	*Minutes.*	
March 11	0	100	171	10 severe.
	5	40	268+	6 severe, 4 mild.
	6	30	259	Do.
	8	20	268	5 severe, 5 mild.
	10	0	----------	7 mild, 3 absent.
March 13	0	100	196	10 severe.
	5	40	269	6 severe, 4 mild.
	6	20	158	6 severe, 3 mild, 1 absent.
	8	10	146	3 severe, 3 mild, 4 absent.
	10	0	----------	2 mild, 8 absent.
March 14	0	100	155	10 severe.
	5	40	264	7 severe, 3 mild.
	6	30	296+	4 severe, 6 mild.
	8	0	----------	1 severe, 4 mild, 5 absent.
	10	0	----------	2 mild, 8 absent.
March 15	0	100	150	10 severe.
	5	0	----------	1 severe, 3 mild, 6 absent.
	6	0	----------	1 mild, 9 absent.
	8	0	----------	10 absent.
	10	0	----------	Do.
March 18	0	90	203	10 severe.
	5	10	364	8 severe, 1 mild, 1 absent.
	6	20	317+	6 severe, 3 mild, 1 absent.
	8	0	----------	3 severe, 4 mild, 3 absent.
	10	0	----------	10 absent.
March 19	0	100	171	10 severe.
	5	20	216	6 severe, 3 mild, 1 absent.
	6	10	201	7 severe, 2 mild, 1 absent.
	8	0	----------	1 severe, 2 mild, 7 absent.
	10	0	----------	4 mild, 6 absent.
March 20	0	100	150	10 severe.
	5	50	284	8 severe, 2 mild.
	6	30	247	7 severe, 3 mild.
	8	10	289	3 severe, 5 mild, 2 absent.
	10	0	----------	5 mild, 5 absent.
March 21	0	80	159	10 severe.
	5	20	288	2 severe, 6 mild, 2 absent.
	6	30	239	5 severe, 5 mild.
	8	10	307	4 severe, 1 mild, 5 absent.
	10	0	----------	1 mild, 9 absent.
March 22	0	80	160	10 severe.
	5	30	333	7 severe, 2 mild, 1 absent.
	6	20	309+	8 severe, 2 mild.
	8	10	269	2 severe, 2 mild, 6 absent.
	10	0	----------	3 mild, 7 absent.
March 25	0	80	186	10 severe.
	5	30	258	6 severe, 4 mild.
	6	30	286	4 severe, 3 mild, 2 absent.
	8	10	339	2 severe, 3 mild, 4 absent.
	10	0	----------	1 severe, 9 absent.

The test has been applied to a fairly large number of commercial lots. The results are given in Table X. It will be seen that, on the whole, the glucose equivalent of commercial preparations does not show very great variations. The exceptional values may partly be due to inaccurate standardization by means of the rabbit method or to deterioration.

The figures in the column headed "Number of rat units found" were obtained as follows: 1 rat unit required 8 grams of glucose per kilo to protect against 1 M. L. D. of insulin, Lot A 2; therefore Lot A 1 which required only 5 grams of glucose to protect against 1

M. L. D. contains less than 1 rat unit, i. e., $8:5=1:x$ or 0.625 rat units. The figures in the last column, "Number of clinical units as calculated from rat test," were obtained as follows: One rat unit is arbitrarily set as equivalent to 16 clinical units. Lot A 2 contains 16 clinical units per c. c. as tested by the rat method. The label, however, states that it contains 12 clinical units per c. c. Lot A 1 tested by the rat method contains 0.625 rat units per c. c.; therefore 1 rat unit : 0.625 rat units = 16 clinical units : x clinical units, or $x=10$ clinical units.

A comparison of the figures presented in the last two columns indicates that insulin brand A shows a maximum difference in potency, as tested by the two methods, of 54 per cent (Lot A 3 being 54 per cent weaker when tested by the rabbit method than when tested by the rat method).

Brand B shows a maximum difference of 60 per cent (Lot B 2 being 60 per cent stronger when tested by the rabbit method than when tested by the rat method). Lot B 3 and B 4 gave the same values with both methods.

TABLE 10.—*Summary of glucose protective test. Commercial preparations. (Standard technique used. At least 10 rats were run on each dose, and 130 rats on lot B 8.)*

Insulin preparation.	Dose of insulin per kilo.	Mortality of control.	Glucose protective dose.	Number of rat units found.	Number of clinical units.	
					As stated on label.	As calculated from rat test.
	c. c.	*Per cent.*	*Gms. per kilo.*			
A 1	1.6	90	5	0.625	16	10
A 2	1.2	100	8	1.00	12	16
A 3	1.2	90	13	1.625	12	26
A 4	2.4	90	10	1.25	24	20
A 5	1.6	100	10	1.25	16	20
B 1	1.6	90	6	0.75	16	12
B 2	1.6	90	5	0.625	16	10
B 3	1.6	98	8	1.00	16	16
B 4	1.6	100	8	1.00	16	16
B 5	1.6	100	10	1.25	16	20
B 6	2.4	95	10	1.25	24	20
B 7	1.6	100	12	1.50	16	14
B 8	1.6	95	10	1.25	16	20

Standardization of an insulin preparation of unknown strength.—The first step in the standardization of an insulin preparation of unknown strength by the rat method is to determine the range of the M. L. D.

Three rats are injected subcutaneously with each of a series of five doses of 100 per cent variation ranging from 1 c. c. to 16 c. c per kilo of body weight. Taking the dose next below that which kills two out of three rats, a series of three doses with 100 per cent variation is run, using 10 rats on each dose. The dose that kills

90 to 100 per cent of the rats is the M. L. D. and is used in the glucose protective test with 5, 6, 8, and 10 grams of glucose per kilo of body weight, respectively, *per os*. This test requires 50 rats—10 receiving the M. L. D. without glucose as a control.

The complete standardization of the insulin preparation requires 95 rats—15 on the first test, 30 on the second, and 50 on the third.

Deterioration.—We have obtained definite indication of deterioration of a large batch of insulin kept under the following conditions: This batch (500 c. c.) was received from the manufacturer February 1, 1924, in a brown glass bottle fitted with rubber stopper. Each cubic centimeter was supposed to contain 20 clinical units. A portion of the contents was removed for another experiment and the bottle was kept in a cold room at 3° C. Beginning March 5, the preparation was used for standardization purposes. Before removing the desired portions needed for the several tests, the bottle was shaken. The sample was taken by means of a pipette which had been cleaned and dried with alcohol and ether. The bottle was returned immediately to the cold room.

During March and April numerous tests gave practically 100 per cent mortality (95 per cent on 160 rats) with 16 clinical units per kilogram body weight. On May 7 the mortality was 70 per cent on 16 units. On May 8, 9, and 10 glucose protective tests were run using 32 units, giving 100 per cent mortality in the controls. On May 12 the mortality test gave 50 per cent with 16 units. In order to determine whether the drop in mortality was due to decrease in toxicity of the drug or to an increased seasonal resistance of the rats, a number of other lots of insulin of which the M. L. D. had been determined previously were retested, with the following negative results:

Preparation.	Clinical units.	M. L. D. mortality.	Date.
	Per kilo.	*Per cent.*	
1	16	100	Apr. 23
		90	May 13
		100	May 15
2	16	100	Apr. 2
		100	Apr. 3
		100	May 14
3	16	100	Apr. 24
		90	May 14
4	24	100	Feb. 18
		100	May 15

Although the standard lot contains 0.4 per cent tricresol as a preservative, the deterioration noted might possibly be attributed to bacterial growth. The sterility of the diluted preparation was tested on nutrient agar plates. Incubation of the latter for 24 and 48 hours showed sterility. In view of the above data it may be concluded that a considerable deterioration of the potency of the

standard insulin solution had taken place, which is evidently not due to bacterial growth, but must be due to some other cause.

The Connaught Antitoxin Laboratories advise the storage of insulin at ordinary room temperature. A toxicity test in our laboratory using one of their lots gave identical results with two portions, one of which had been stored at a temperature of 3° C. and the other at laboratory room temperature (approximately 68° F.) for 40 days prior to testing.

Discussion.

In our experience the mortality test as described yields a good estimate of the potency of insulin, but we believe that the combination of the mortality and glucose protective test forms an even better foundation for the biological standardization of this drug. The combination of the two tests should insure the estimation of the specific action of insulin in terms of glucose. It is obvious that any technique which allows the accurate estimation of the glucose equivalent is very highly desirable. Completely depancreatized dogs or clinical cases of diabetes are not so suitable for this purpose as the standardized rat. Work on the depancreatized dog is rather difficult, both technically and for the reason that it is difficult to adjust the metabolism of these animals in a satisfactory manner for long periods of time. Human diabetics, on the other hand, vary in their glucose equivalent from case to case according to the degree of deviation of their metabolism from the normal. This is shown very clearly by the various figures given for the clinical glucose equivalent.

Woodyatt (1922) obtained a maximum utilization of 1.0 to 1.5 grams of glucose per clinical unit of insulin on carefully selected diabetics. The literature accompanying insulin manufactured by the Connaught Antitoxin Laboratories states that one clinical unit will enable a diabetic to use 1 to 4 grams additional glucose, depending on the severity of the case. The product of Eli Lilly & Co. is claimed to allow the utilization of 1.5 to 2 grams additional glucose per unit.

Ringer (1923), working with the completely phloridzinized dog, finds that one clinical unit yields a maximum oxidation of 0.95 grams of glucose per clinical unit. Allan (1924) established the glucose equivalent on the completely depancreatized dog, and found that 16 clinical units of insulin cause the utilization of 7 grams glucose.

It is of interest in this connection to compare the glucose equivalent of insulin as determined in the rats, with the figures mentioned above. According to definition, 16 clinical units should be completely antagonized by 8 grams of glucose in the rat, or one clinical unit by 0.5 grams. This latter figure is therefore the glucose equivalent in rats as obtained by our method. It will be noted that this

figure is lower than any of the figures for glucose equivalents given above (with the exception of Allan's figure), and this is easily explained by the fact that the amount of glucose required to protect against death is naturally lower than the dose of glucose which would keep the carbohydrate metabolism at the normal level.

All of the commercial lots of insulin studied by us had been standardized on rabbits and tested on selected cases of diabetes. The fact that the rat test on the whole confirmed the findings obtained on rabbits and human beings is strong presumptive evidence of the reliability of the rat test. In subsequent communications we shall submit further evidence of the reliability of the rat test and its usefulness in the study of certain phases of intermediate metabolism and the antagonistic action of insulin on certain other endocrine products. There is only one question which remains to be settled, and that is whether different strains of rats will give different values. If so, the adoption of the suggestion made by the Edinburgh conference of the use of a standard insulin powder should overcome this difficulty. The technique of the test is simple and the expense involved is probably less than that involving the use of a large number of rabbits. In order to economize on the number of animals we have found that it is permissible to use for preliminary work on a preparation of unknown potency, rats which had shown only mild symptoms on previous tests and which had not received insulin less than 10 days previously. Even rats having recovered after severe symptoms can be used, though they seem to show an increased susceptibility, as indicated by a lower M. L. D. Rats of a greater weight than 100 to 120 grams may also be used for a preliminary assay, but we have the impression that the susceptibility of rats is affected somewhat by age.

An important advantage in work with rats is their great resistance to infectious diseases, provided they are cared for properly; we had a great deal of difficulty on this score with rabbits. Mice are very susceptible to the ravages of mouse typhoid epidemics.

The fact that rats require a larger dose of insulin per kilogram body weight than do rabbits and mice is no serious disadvantage.

The accuracy of the rat test insures a maximum error of 20 per cent, and this is perfectly permissible in biological standardization.

The average commercial preparation released by the Insulin Committee will require 16 clinical units per kilogram body weight to produce a mortality of 90 to 100 per cent in rats. About 8 grams of glucose per kilogram are required to protect 100 per cent of rats from death when injected with 16 clinical units of insulin per kilogram body weight. This, then, should be the requirement of preparations for clinical use tested by our method.

Conclusions.

1. Albino rats respond to insulin in the same manner as do other animals. The symptoms are: Increasing weakness followed by coma. Occasionally rolling convulsions are noted similar to those observed in rabbits. Death is preceded by respiratory failure.

2. The toxicity of insulin in rats shows marked differences according to method of administration of the drug. The toxicity is greatest with subcutaneous injections, lower with intravenous, and lowest with intraperitoneal injection.

3. The frequency curve of the blood sugar of rats kept on a standard diet, followed by a period of starvation of 18 hours, was determined. This curve shows that the standard deviation is much smaller than in the case of rabbits.

Severe symptoms produced by a subcutaneous injection of insulin into standardized rats are accompanied by a fall of blood sugar from an average value of 113 milligrams per 100 c. c. blood before injection to 50 milligrams.

4. The glycogen content of the liver of standardized rats shows differences according to the method used for killing the animals. If the rats are bled to death, the liver contains 0.053 per cent of glycogen and skeletal muscle 0.09 per cent. Insulin given in sufficient amount to produce severe symptoms lowers the liver glycogen 49 per cent and the muscle glycogen 60 per cent.

5. There is a considerable individual variation in susceptibility to insulin in rats kept under standardized conditions. For this reason it is advisable to use not less than 10 animals on each dose for purposes of bio-assay.

6. The percentage of mortality increases very considerably by increasing the atmospheric temperature at which the aninals are kept from 15° C. to 29° C.

7. A method is described which permits the determination of the minimum lethal dose of insulin in standardized rats. A further test (glucose protective test) was elaborated for the determination of the glucose equivalent of insulin.

8. These methods were used for the bio-assay of various commercial insulin preparations, and insulin prepared by the authors. The results indicate a considerable variation in potency of commercial lots. If the test is properly carried out, the error in the result should not exceed 20 per cent.

9. Evidence of deterioration as a result of storage of insulin was obtained only in one case.

10. In order to conform with the present strength of the average product released by the Insulin Committee of the University of Toronto, the requirements of preparations tested by the rat method should be as follows: The M. L. D. is the lowest dose per kilogram body

weight which will cause a mortality of 90 to 100 per cent in a series of animals. This dose would correspond to 16 clinical units per kilogram body weight. Furthermore, 8 grams glucose per kilogram body weight given *per os* at the time of the subcutaneous injection of the M. L. D. of insulin should protect all of the animals so injected from death.

The glucose equivalent as thus defined is therefore 0.5 grams per clinical unit.

References.

Allan, F. M. (1924): Amer. Jour. Physiol., LXVII, 275.
Banting, Best, Collip, Macleod, and Noble (1922): Amer. Jour. Physiol., LXII, 162.
Blatherwick, Long, Bell, Maxwell, and Hill (1924): Jour. Biol. Chem., LIX—Proceed. Am. Soc. Biol. Chemists.
Clough, H. D., Allen, R. S., and Root, E. W. (1923): Am. Jour. Physiol., LXVI, 461.
Eadie, G. S., and Macleod, J. J. R. (1923): Am. Jour. Physiol., LXIV. 285.
Fraser, Donald T. (1923): Jour. Lab. & Clin. Med., VIII, 425.
Macleod, J. J. R. (1924): Physiol. Reviews, IV, 21.
Macleod, J. J. R., and Orr, M. D. (1924): Jour. Pharmacol. & exp. Ther., XXIII, 137. Proceed.
Myers, V. C., and Bailey, C. V. (1916): Jour. Biol. Chem., XXIV, 147.
Osborne, Th. B., and Mendel, L. B. (1924): Jour. Biol. Chem., LIX, 13.
Ringer, M. (1923): Jour. Biol. Chem., LVIII, 483.
Scott, E. L., and Ford, Th. H. (1923): Am. Jour. Physiol., LXIII, 520.
Voegtlin, Carl, and Dunn, Edith R. (1923): Pub. Health Rep., 38, 1747. (Reprint No. 855.)

THE PRESENT STATUS OF THE PARASITIC NEMATODE FAMILY *ASCARIDAE*.

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The nematode genus *Ascaris* Linn., 1758, represented by the common lumbricoid worm of man, contains so many and so varied species that they have gradually been assorted into three superfamilies, several families, and numerous genera. Gradually the genus *Ascaris* came to be restricted to parasitic nematodes with 3 lips. During the past few years the 3-lipped ascarids have been considered to represent a special family, which has been divided into various subfamilies and a number of genera. The literature in question is scattered in medical, veterinary, and zoological periodicals in North and South America, England, France, Belgium, and Russia, and is completely accessible to very few workers.

Since this group of parasites is of importance not only from a standpoint of human as well as of comparative medicine, and since it also has its rôle in international diplomatic correspondence, it seems desirable from a standpoint of applied science, independent of the

question of pure science, to bring the various genera together in one place, for ready reference.

Naturally, some of the genera are too recent to permit of prophecy as to their probable permanency.

The following key gives the more essential characters of the present genera of the family ASCARIDAE as now restricted; at least five of these genera (*Ascaris*, *Toxocara*=*Belascaris*, *Toxascaris*, *Lagochilascaris*, and *Fusaria* sensu lato) are reported as parasitic in man.

1(6) Immature forms which can not be allocated to well-defined modern genera. See 2.

2(3) *Agamo-ascaris* Stiles & Brown, 1924.—A general collective genus for immature forms; chiefly encysted stages; no genotype is necessary.

3(2) Larval genera with definite genotypes; these may therefore eventually become valid genera; present status sub judice. See 4.

4(5) *Capsularia* Goeze in Zed., 1800a, 5, 7–15.—Esophagus with distinct ventriculus. Tsd. tat. *salaris*=*Ascaris capsularia* from *Salmo salar*. Syn. *Stomachus* Goeze in Zed., 1800a, 11, mt. *albus* (generic and specific names refer to the white ventriculus)=*salaris* renamed. This genus seems to belong in the ANISAKINAE, with the possibility that it may eventually supplant one of the other genera; *Anisakis* and *Porrocaecum* seem to come into special consideration. This point can be determined only on basis of European material from *Salmo salar*. Not Capsularia Oken, 1815, coleopteron.

5(4) *Filocapsularia* Deslgch., 1824q.—Based on *Filocapsularia communis* in fish.

6(1) More or less mature forms. See 7.

7(8) *Fusaria* Zed., 1800a, sensu lato.—Ascarids of uncertain generic position. Theoretically this is an objective synonym of *Ascaris*. Practically it is a collective genus in the sense of *Ascaris* sensu lato. In order that *Ascaris* s. str., type *lumbricoides*, may be restricted to a natural generic group, and no longer lose its taxonomic significance by being used as a collective group it is suggested that *Fusaria* s. l. be used as the collective group in which to place ascarids which can not be located generically in the restricted genera. See 8.

8(7) Ascarids of fairly certain systematic position in genera which have at present a restricted status. See 9.

9(55) Subfamily position fairly well recognized. See 10.

10(12) GOEZIINAE Baylis, 1920, P, 263.—Body with rings of cuticular spines (see also 56). Post-labial fringe and post-labial longitudinal ridges absent. Syn. Goezinae Trav., 1920a.

11 *Goezia* Zed., 1800a.—Interlabia and alae absent. Lips flattened. Esophageal appendix long; intestinal cecum short. Type *armata*=*ascaroides* from *Silurus*. Syn. *Lecanocephalus* Dies., 1839a, mt. *spinulosus*.

12(10) Body without rings of cuticular spines. See 13.

13(16) HETEROCHEILINAE Rail. & Henry, 1912.—Several raised longitudinal cuticular ridges immediately post-labial. Intestinal cecum present. Post-labial fringe absent. See 14.

14(15) *Heterocheilus* Dies., 1839a.—Dorsal lip longer and quite unlike the 2 symmetrical ventral lips. Post-labial ridges 9. Esophageal bulb present (not shown in original figure of type species). Spicules 2, alate. Uteri 2. Mt. *tunicatus* s. *heterolobus*, from *Manatus*. Syn. *Lobocephalus* Dies., 1838a, mt. *heterolobus*.

15(14) *Typhlophoros* Linst., 1906.—Alae absent. Post-labial ridges 16. Mt. *lamellaris* from *Gavialis.*

16(13) Post-labial longitudinal cuticular ridges absent. See 17.

17(19) CROSSOPHORINAE Baylis, 1920, P, 263.—Post-labial margin with fringe.

18 *Crossophorus* Ehrenb., 1828.—Alae absent. Intestinal ceca 2, anterior. Male with 1 spiculum. Type *collaris.*

19(17) Post-labial margin without fringe. See 20.

20(38) ANISAKINAE Rail. & Henry, 1912.—Muscular esophagus separated from intestine by a non-muscular ventriculus (so that esophagus is divided tandem); or if ventriculus is absent, intestinal cecum is present. General appearance like *Ascaris,* i. e., smooth cuticle, transversely striated but without cuticular spines or other raised structures. Anterior cecum absent or present (springing from intestine and lying along side of esophagus); posterior cecum or solid glandular appendix absent, or present, developed in connection with the ventricular portion of esophagus. Interlabia and dentigerous ridges present or absent. Parasitic in intestine chiefly of aquatic or at least of piscivorous mammals, birds, reptiles, and fishes; larval stage encysted in fishes. See 21. See also 4, *Capsularia.*

21(31) Non-muscular ventriculus present; esophagus without distinct muscular bulb; alae absent. See 22.

22(25) Ventriculus without esophageal appendix. See 23.

23(24) *Anisakis* Duj., 1845a.—Intestinal cecum, esophageal bulb and appendix, and interlabia absent. Dentigerous ridge present. Type *dussumierii* =simplex (misdetermined).

24(23) *Porrocaecum* Rail. & Henry, 1912.—Intestinal cecum, interlabia, and dentigerous ridge present. Esophageal bulb and appendix absent. Mt. *crassum.* Syn. *Terranova* Leiper & Atkinson, 1914 (tod. *antarctica* from *Mustelus*), fide Baylis, 1920, P, 258; but L. & A. report "no interlabia" for the genotype.

25(22) Ventriculus with esophageal appendix. See 26.

26(28) Intestinal cecum absent. See 27.

27 *Raphidascaris* Rail. & Henry, 1915.—One esophageal appendix and 3 interlabia present. Dentigerous ridge absent. Tod. *acus.*

28(26) Intestinal cecum present. See 29.

29(30) *Contracaecum* Rail. & Henry, 1912.—One esophageal appendix present. Interlabia present. Dentigerous ridge and esophageal bulb absent. Tod. *spiculigerum.* Syn. *Kathleena* Leiper & Atkinson, 1914, tod. *osculata.*

30(29) *Multicaecum* Baylis, 1923, P, 230.—5 esophageal appendices present (2 anterior, 3 posterior). Interlabia small, with well-marked grooves running to bases of lips. Dentigerous ridges present. Cervical papillae not prominent, considerably behind nerve-ring. Excretory pore slightly behind nerve-ring. Tail of male without definite alae. Spicules 2, equal; gubernaculum somewhat resembling that of *Dujardinia;* caudal papillae few, arranged much as in *Dujardinia.* Vulva about equatorial; muscular vagina and unpaired portion of uterus run caudad; the 2 branches of uterus very short, and so narrow near the bifurcation as to contain only a single row of eggs. Eggs with thin, finely granulated shell, of oval shape, with contents segmenting when ready for laying. Tod. *agile* from *Crocodilus.*

31(21) Ventriculus and esophageal appendix absent. Intestinal cecum present. See 32.

32(35) Esophageal bulb present. See 33.

33(34) *Hysterothylacium* Ward & Magath, 1917.—Narrow alae present. Body without anterior tunic. Lips not prominent. Esophagus long, slender, with terminal spherical bulb. Intestine with short simple cecum directed caudad. Spicules 2, equal; papillae?. Female unknown. Mt. *brachyurum*.

34(33) *Dujardinia* Ged., 1916, Rza, 21.—Alae absent. Interlabia present. Dentigerous ridge absent. Esophagus with small posterior spherical bulb. Intestinal cecum present. No esophageal appendix. Lips with cuticle of their internal surfaces produced into large toothlike structures apparently capable of being interlocked; these structures are carried by 3 main cuticular lobes on anterior border of each lip. Well-marked cuticular grooves run from interlabia to bases of lips. Cuticle of body usually thin, with very fine and faint transverse striation. A pair of cervical papillae present at some distance behind nerve-ring. Excretory pore at level of nerve-ring. Tail of male with rather well-marked lateral alae extending for short distance in region of cloaca; caudal papillae few; spicules 2, equal, slender; gubernaculum usually present, of characteristic shape, with expanded and solid head at proximal end, and hollow and tapering distally; lumen of distal portion has opening on posterior surface of organ. Vulva pre-equatorial, opening into muscular, almost suckerlike "atrium" (in genotype) from which the very long slender vagina runs mainly caudad; vagina ends in small, expanded egg-chamber, from which are given off caudad the 2 uterine branches, narrow and coiled at first, but expanding more posteriorly into 2 very voluminous and thin-walled tubes, filled with eggs in mature individuals and running parallel to each other. Ova with very thin, membranous shell, roundish-oval or subglobular in shape, and with contents unsegmented up to time of laying, and usually separated by a large space from the shell. Tod. *helicina* from *Crocodilus*. Compare 47.

35(32) Esophageal bulb absent. Dentigerous ridge present. See 36.

36(37) *Amplicaecum* Baylis, 1920, P, 262.—Small interlabia present. Intestinal cecum wide. Esophageal ventriculus, bulb, and appendix absent. Tod. *colurum* from *Lophaëtus*.

37(36) *Angusticaecum* Baylis, 1920, P, 262.—Interlabia absent. Intestinal cecum long, slender, originates slightly post-esophageal. Esophageal ventriculus and appendix absent. Tod. *holopterum* from *Testudo*.

38(20) ASCARINAE Trav., 1913.—Ventriculus, esophageal appendix, and intestinal cecum absent. Esophagus entirely muscular, with or without posterior bulb. Interlabia and alae absent or present. At least some of the genera do not require an intermediate host. See 39.

39(44) Cephalic alae present. See 40.

40(43) Alae confined to head, giving arrow-shaped head. Interlabia absent. See 41.

41(42) *Toxocara* Stiles, 1905.—Esophageal bulb present. Oral end bent ventrad. Cuticle coarsely striated. Tail of male conical; a papillae-bearing protuberance post-anal. Testis pre-equatorial. Vulva pre-equatorial. Eggs corrugated. Development without intermediate host. Tod. *canis*, renamed *werneri*, renamed *marginata*, from dogs. Syn. *Belascaris* Leiper, 1907, tod. *mystax=cati*.

42(41) *Toxascaris* Leiper, 1907.—Esophageal bulb absent. Oral end bent dorsad. Cuticle finely striated. Tail of male tapers to a point. Testis somewhat post-equatorial. Vulva about equatorial. Eggs oval, smooth. Tod. *leonina*.

43(40) *Lagochilascaris* Leiper, 1909.—Alae extend entire length of body. Thick lips separated by furrow from body; small interlabia without "pulp"; the cutting angle of each lip bifurcated. Eggs thick shelled with mosaic pattern. Mt. *minor*.

44(39) Cephalic alae absent. See 45.

45(48) Interlabia present. See 46.

46(47) *Ophidascaris* Baylis, 1921, P, 412.—Lips almost square, with more or less rounded angles, and generally as broad as long; dorsal lip slightly smaller than ventro-lateral lips; interlabia usually well-developed; from the interlabia deep transverse grooves in cuticle run partially around the bases of main lips towards their main axes. Esophagus relatively short, without bulb or ventriculus; neither esophageal nor intestinal cecum (the intestine, however, is frequently pushed up into an annular "cecum" around the posterior end of esophagus). Vagina and uterus run caudad; uterus with two parallel branches; vulva usually post-equatorial; and genital organs (in both sexes) usually confined post-equatorially, often causing fusiform thickening. Tod. *filaria* from *Python*.

47(46) *Trispiculascaris* Skrj., 1916, 123.—Gubernaculum present. Small body with rather large lips provided with auricular outgrowths on the sides; dentigerous ridge and interlabia present. Esophagus and intestine simple, without blind diverticula. Tail of male strongly bent and provided with wide alae and very few preanal and postanal papillae arranged in one row on each side of body; 2 fine, thin spicula, equal. Tail of female straight, conically pointed. Vulva pre-equatorial. Parasitic in alimentary tract of reptiles. Mt. tod. *helicina* Mol. of Skrj., from *Crocodilus*. Note that *Dujardinia* (34) is based upon *helicina* which is reported as having an intestinal cecum. Possibly there is a confusion in specific determination of specimens.

48(45) Interlabia absent. See 49.

49(52) Uteri more than 2. See 50.

50(51) *Polydelphis* Duj., 1845a.—Uteri 4. A rudimentary cecum sometimes present. Esophageal bulb and ventriculus absent. Mt. *anoura*.

51(50) *Hexametra* Trav., 1920a, 64.—Uteri 6. Dentigerous ridge present. Esophageal bulb and cecum absent. Intestinal cecum absent. Tod. *hexametra* from *Chamaeleo dilepis*.

52(49) Uteri 2. See 53.

53(54) *Orneoascaris* Skrj., 1916, 124.—Tail of male with broad alae. Dentigerous ridge present. Body of medium size. Large lips, 3; interlabia absent. Alimentary tract simple, without ceca. Tail of male with lateral, wide, alae; spicules 2, equal, of a very delicate structure; gubernaculum absent; preanal papillae not numerous, pedunculate (7 pairs), their free end resembling the crown of a double flower, consisting of a complex of petal-shaped lobes; postanal papillae sessile; venter of tail of male marked both in longitudinal and in transverse directions with series of furrows which form a fine mosaic network of stellate loops; this network partly prealate. Vulva preequatorial. Large oval eggs. Parasitic in intestines of Amphibia. Mt. *chrysanthemoides* from *Bufo* species, Brit. E. Africa.

54(53) *Ascaris* s. str. Linn., 1758a.—Tail of male without alae. Dentigerous ridge present. Esophageal bulb and appendix, and intestinal cecum absent. Spicules 2, equal; tail of male with numerous ventral preanal and postanal papillae. Vulva nearly equatorial or preequatorial. Eggshell thick, usually with numerous mamillate projections on its outer albuminous layer. Parasitic in intestine of mammals. Development without intermediate host. Tsd. *lumbricoides* from *Homo*.

55(9) Subfamily position sub judice. See 56.

56(57) *Echinonema* Linst., 1898b.—Secernentes, polymyaria: Rings of spines about body. Spicules 2, equal, rather short. Head end thickened, armed with 2 rings of rather long, sharp spines; neck short, unarmed, narrower than head; followed by rings of shorter thorns which pierce the skin; this spinose armature extends caudad to twice length of esophagus; then follow rings of very fine spines which extend to caudal end. Mouth opening triangular without papillae. Esophagus muscular, (pictured) not divided tandem and without bulb and ceca; intestine (pictured) without ceca. Nerve ring in swollen head portion. Tail of male acutely pointed; papillae on tail end of male, 3 pairs preanal, 3 pairs postanal papillae and 1 pair adanal papillae. Vulva preequatorial on border between 1st and 2d fourths. Eggs globular, thick-shelled prior to division; later when embryonated the shell becomes relatively thinner. Mt. tod. *cinctus*. Syn. Hoplocephalus Linst., 1898a, renamed.

57(56) Body without rings of spines, at least these are not reported. Spicule single. See 58.

58(59) *Acanthocheilus* Mol., 1858d.—?ASCARIDAE: Spicule 1, short, arched, with knob on free extremity. Lips 3, with semicircular free margin, each lip bearing a median, rather centrally located papilla and 4 spines arranged in pairs, 1 pair each side of midline of lip and each pair pointing toward and practically engaging the nearer pair of adjoining lips. Interlabia absent. Head of slightly greater diameter than neck and circular in view en face. Body ascaridiform, cylindrical, about 20 to 60 mm. long. Esophagus composed of 4 distinct tandem regions, (1) an anterior swollen portion, (2) a narrower portion, (3) a second swollen portion and (4) a distinct striated (hence muscular) bulb; no glandular ventriculus, diverticulum, or cecum shown in published illustrations. Cuticle with fine transverse striations, without spines or fringe. Tail awl-shaped. Anal zone of tail of male much thicker than postanal zone, and anus (*A. bicuspis*) said to be lateral near a precaudal prominence. Vulva preequatorial. Eggs about 52 μ, with more or less pentagonal to hexagonal shell which shows undulating striations. Mt. *quadridentatus* from *Mustelus plebejus*.

59(58) *Heligmus* Duj., 1845a.—Spicule 1, very long, flexible, can form a helix spiral and formed of transparent striated tube. Body cylindrical, slightly attenuate toward extremities. Head obtuse. Lips not very distinct. Esophagus muscular, swollen; "ventricule distinct" [=? ventricule or ? bulb]. [No mention of spines, ridges, fringes, ceca.] Tail of male inflexed, conical, with double row of ventral papillae. Anus on prominent tubercle. Vulva preequatorial. Mt. *longicirrus* from *Pleuronectes platessa*.

Examinations for Entrance Into the Regular Corps of the United States Public Health Service.

Examinations of candidates for entrance into the Regular Corps of the United States Public Health Service will be held at the following-named places on the dates specified:

Washington, D. C., September 15, 1924.
Chicago, Ill., September 15, 1924.
San Francisco, Calif., September 15, 1924.
New Orleans, La., September 15, 1924.

Candidates must be not less than 23 nor more than 32 years of age, and they must have been graduated in medicine at some reputable medical college, and have had one year's hospital experience or two years' professional practice. They must pass satisfactorily, oral, written, and clinical tests before a board of medical officers and undergo a physical examination.

Successful candidates will be recommended for appointment by the President with the advice and consent of the Senate.

Requests for information or permission to take this examination should be addressed to the Surgeon General, United States Public Health Service, Washington, D. C.

DEATHS DURING WEEK ENDED JULY 26, 1924.

Summary of information received by telegraph from industrial insurance companies for week ended July 26, 1924, and corresponding week of 1923. (From the Weekly Health Index, July 29, 1924, issued by the Bureau of the Census, Department of Commerce.)

	Week ended July 26, 1924.	Corresponding week, 1923.
Policies in force	56, 612, 880	52, 979, 683
Number of death claims	9, 508	8, 504
Death claims per 1,000 policies in force, annual rate	8. 8	8. 5

Deaths from all causes in certain large cities of the United States during the week ended July 26, 1924, infant mortality, annual death rate, and comparison with corresponding week of 1923. (From the Weekly Health Index, July 29, 1924, issued by the Bureau of the Census, Department of Commerce.)

City.	Week ended July 26, 1924.		Annual death rate per 1,000 corresponding week, 1923.	Deaths under 1 year.		Infant mortality rate, week ended July 26, 1924.[2]
	Total deaths.	Death rate.[1]		Week ended July 26, 1924.	Corresponding week, 1923.	
Total (62 cities)	5,654	11.0	[3] 10.9	722	[3] 782	
Akron	30			5	1	53
Albany [4]	34	15.0	13.3	3	3	68
Atlanta	97	22.2	22.2	15	16	
Baltimore [4]	167	11.1	12.4	21	32	63
Birmingham	59	15.3	19.2	10	21	
Boston	166	11.1	11.3	25	20	69
Bridgeport	33			2	3	32
Buffalo	124	11.9	10.0	12	9	51
Cambridge	19	8.9	11.2	2	1	35
Camden	32	13.2	14.7	3	6	49
Chicago [4]	565	10.0	9.6	72	81	67
Cincinnati	113	14.4	14.2	15	14	94
Cleveland	151	8.6	8.3	21	16	53
Columbus	67	13.1	13.2	6	8	57
Dallas	39	10.8	15.4	2	10	
Denver	53			2	10	
Des Moines	33	11.9	7.4	5	0	
Detroit	207			28	40	52
Duluth	13	6.3	7.8	3	3	65
Erie	23			1	0	21
Fall River [4]	28	12.1	12.9	5	6	70
Flint	15			2	3	35
Fort Worth	28	9.9	8.0	2	2	
Grand Rapids	37	13.0	5.4	3	1	47
Houston	44			12	8	
Indianapolis	89	13.2	14.8	10	11	74
Jacksonville, Fla	43	21.9	17.7	6	6	

[1] Annual rate per 1,000 population.
[2] Deaths under 1 year per 1,000 births—an annual rate based on deaths under 1 year for the week and estimated births for 1923. Cities left blank are not in the registration area for births.
[3] Data for 60 cities.
[4] Deaths for week ended Friday, July 25, 1924.

Deaths from all causes in certain large cities of the United States during the week ended July 26, 1924, infant mortality, annual death rate, and comparison with corresponding week of 1923. (*From the Weekly Health Index, July 29, 1924, issued by the Bureau of the Census, Department of Commerce.*)

City.	Week ended July 26, 1924.		Annual death rate per 1,000 corresponding week, 1923.	Deaths under 1 year.		Infant mortality rate, week ended July 26, 1924.
	Total deaths.	Death rate.		Week ended July 26, 1924.	Corresponding week, 1923.	
Jersey City	77	12.9	10.8	10	12	71
Kansas City, Kans.	21	9.3	10.8	1	2	19
Kansas City, Mo.	87	12.6	12.4	6	17	
Los Angeles	177			16	24	50
Louisville	72	14.5	15.6	8	17	75
Lowell	27	12.2	9.1	7	9	125
Memphis	106	32.1	19.9	23	14	
Milwaukee	67	7.1	9.5	13	14	62
Minneapolis	93	11.6	10.2	5	5	27
Nashville [4]	43	18.2	17.9	6	5	
New Bedford	16	6.3	10.0	0	5	0
New Haven	44	13.0	9.9	9	4	119
New Orleans	176	22.4	17.1	22	19	
New York	1,068	9.3	9.4	135	142	55
Bronx Borough	117	7.0	8.5	10	11	35
Brooklyn Borough	361	8.6	8.2	59	61	63
Manhattan Borough	462	10.6	10.5	47	56	48
Queens Borough	91	8.6	9.6	16	9	81
Richmond Borough	37	14.8	12.3	3	5	55
Newark, N. J.	87	10.2	10.2	12	21	56
Norfolk	32	10.2	13.1	8	6	143
Oakland	46	9.7	6.9	6	6	75
Oklahoma City	13	6.5		1		
Omaha	39	9.8	8.9	8	7	86
Paterson	31	11.5	9.7	3	2	51
Philadelphia	377	10.1	11.4	49	52	63
Pittsburgh	132	11.0	11.2	30	19	102
Portland, Oreg.	43	8.1	12.0	3	5	31
Providence	55	11.8	14.2	8	15	65
Richmond	56	15.9	17.3	9	13	109
Rochester	65	10.4		9		71
St. Louis	180	11.5	10.6	17	20	
St. Paul	53	11.3	10.6	7	6	60
Salt Lake City [4]	29	11.8	9.9	2	4	40
San Antonio	43	11.7	13.0	9	9	
San Francisco	123	11.7	12.2	3	10	18
Schenectady	20	10.4	5.3	0	1	0
Seattle	60			3	5	29
Somerville	17	8.8	5.3	4	1	109
Spokane	17			3	3	66
Springfield, Mass.	28	9.8	10.8	6	9	101
Tacoma	19	9.6	10.8	1	2	24
Toledo	60	11.3	8.5	7	7	66
Trenton	37	14.9	12.7	4	3	67
Utica	21	10.4	8.1	3	0	65
Washington, D. C.	123	13.2	13.0	14	16	81
Waterbury	16			2	2	46
Wilmington, Del.	38	16.5	12.0	6	3	134
Worcester	38	10.1	11.7	2	5	24
Yonkers	14	6.7	6.3	1	1	22
Youngstown	34	11.4	13.5	4	8	55

PREVALENCE OF DISEASE.

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring.

UNITED STATES.

CURRENT WEEKLY STATE REPORTS.

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers.

Reports for Week Ended Aug. 2, 1924.

ARIZONA.	Cases.
Chicken pox	7
Measles	1
Scarlet fever	3
Typhoid fever	1

ARKANSAS.	
Chicken pox	3
Diphtheria	3
Influenza	17
Malaria	103
Measles	20
Mumps	7
Pellagra	7
Scarlet fever	1
Trachoma	1
Tuberculosis	2
Typhoid fever	45
Whooping cough	15

COLORADO. (Exclusive of Denver.)	
Chicken pox	2
Diphtheria	4
Measles	1
Mumps	2
Pneumonia	1
Rabies	1
Scarlet fever	3
Smallpox	1
Tuberculosis	32
Typhoid fever	2
Whooping cough	15

CONNECTICUT.	
Cerebrospinal meningitis	2
Chicken pox	16
Diphtheria	21
Dysentery (bacillary)	3
Influenza	2
Lethargic encephalitis	1
Malaria	5
Measles	24
Mumps	18
Pneumonia (lobar)	4
Poliomyelitis	6
Scarlet fever	19
Trahoma	1
Tuberculosis (all forms)	39
Typhoid fever	8
Whooping cough	41

DELAWARE.	Cases.
Cerebrospinal meningitis	1
Diphtheria	2
Measles	3
Mumps	2
Scarlet fever	6
Tuberculosis	3
Typhoid fever	3
Whooping cough	4

FLORIDA.	
Diphtheria	9
Malaria	40
Typhoid fever	10

GEORGIA.	
Cerebrospinal meningitis	1
Chicken pox	2
Diphtheria	7
Dysentery (bacillary)	17
Hookworm disease	7
Malaria	32
Measles	1
Mumps	4
Paratyphoid fever	4
Pellagra	5
Pneumonia	10
Smallpox	2
Tuberculosis (all forms)	26
Typhoid fever	42
Whooping cough	18

ILLINOIS.	
Diphtheria:	
Cook County	32
Scattering	19
Measles	132
Pneumonia	59
Poliomyelitis:	
Cook County	2
Marion County	1
St. Clair County	1
Scarlet fever:	
Cook County	32
Scattering	30
Smallpox	12
Tuberculosis	340
Typhoid fever	34
Whooping cough	214

KANSAS.

	Cases.
Cerebrospinal meningitis	1
Chicken pox	4
Diphtheria	17
Influenza	2
Lethargic encephalitis	1
Measles	18
Mumps	30
Pneumonia	10
Poliomyelitis	1
Scarlet fever	28
Septic sore throat	1
Smallpox	7
Tetanus	1
Tuberculosis	33
Typhoid fever	13
Whooping cough	38

LOUISIANA.

Diphtheria	13
Hookworm disease	11
Malaria	29
Measles	5
Pneumonia	12
Scarlet fever	3
Smallpox	6
Tuberculosis	33
Typhoid fever	35

MAINE.

Chicken pox	8
Diphtheria	5
German measles	2
Measles	8
Mumps	9
Poliomyelitis	1
Scarlet fever	18
Smallpox	1
Tuberculosis	7
Typhoid fever	8
Whooping cough	18

MARYLAND.[1]

Chicken pox	2
Diphtheria	20
German measles	1
Influenza	12
Malaria	2
Measles	27
Mumps	3
Ophthalmia neonatorum	1
Pneumonia (all forms)	15
Poliomyelitis	6
Scarlet fever	11
Tuberculosis	44
Typhoid fever	22
Whooping cough	63

MASSACHUSETTS.

Cerebrospinal meningitis	2
Chicken pox	24
Conjunctivitis (suppurative)	12
Diphtheria	77
German measles	5
Hookworm disease	2
Influenza	4

MASSACHUSETTS—continued.

	Cases.
Measles	67
Mumps	33
Ophthalmia neonatorum	21
Pellagra	3
Pneumonia (lobar)	19
Poliomyelitis	3
Scarlet fever	68
Septic sore throat	7
Trachoma	3
Tuberculosis (all forms)	117
Typhoid fever	9
Whooping cough	54

MICHIGAN.

Diphtheria	57
Measles	49
Pneumonia	22
Scarlet fever	104
Smallpox	37
Tuberculosis	68
Typhoid fever	26
Whooping cough	117

MONTANA.

Diphtheria	3
Poliomyelitis:	
Anaconda	1
Missoula	1
Rocky Mountain spotted fever:	
Musselshell	1
Scarlet fever	10
Smallpox	7
Tularaemia—Hamilton	1
Typhoid fever	1

NEW JERSEY.

Cerebrospinal meningitis	1
Chicken pox	26
Diphtheria	49
Measles	67
Pneumonia	37
Poliomyelitis	1
Scarlet fever	29
Smallpox	3
Typhoid fever	15
Whooping cough	230

NEW MEXICO.

Diphtheria	10
Measles	3
Mumps	2
Tuberculosis	10
Typhoid fever	2
Vincent's angina	2

NORTH CAROLINA.

Chicken pox	4
Diphtheria	52
Measles	43
Poliomyelitis	2
Scarlet fever	16
Septic sore throat	2
Smallpox	14
Typhoid fever	97
Whooping cough	155

[1] Week ended Friday.

OREGON.	Cases.
Chicken pox	13
Diphtheria:	
Portland	12
Scattering	7
Malaria	1
Measles	3
Mumps	2
Pellagra	[1] 1
Pneumonia	[1] 4
Scarlet fever	6
Septic sore throat	6
Smallpox:	
Portland	8
Scattering	2
Tuberculosis	10
Typhoid fever	3
Whooping cough	2

TEXAS.	
Cerebrospinal meningitis	1
Chicken pox	4
Diphtheria	8
Influenza	3
Measles	10
Mumps	4
Paratyphoid fever	1
Pellagra	2
Pneumonia	2
Scarlet fever	17
Smallpox	10
Tuberculosis	38
Typhoid fever	8
Typhus fever	1
Whooping cough	33

VERMONT.	
Chicken pox	4
Diphtheria	1
Measles	17
Mumps	3
Scarlet fever	5
Typhoid fever	1
Whooping cough	6

VIRGINIA.	Cases.
Poliomyelitis—Spotsylvania County	1

WASHINGTON.	
Chicken pox	15
Diphtheria	18
Measles	6
Mumps	5
Poliomyelitis:	
King County	1
Kittitas County	1
Scarlet fever	26
Smallpox	23
Tuberculosis	4
Typhoid fever	8
Whooping cough	6

WISCONSIN.	
Milwaukee:	
Cerebrospinal meningitis	1
Chicken pox	21
Diphtheria	8
Measles	16
Mumps	9
Pneumonia	1
Tuberculosis	20
Typhoid fever	1
Whooping cough	27
Scattering:	
Cerebrospinal meningitis	2
Chicken pox	35
Diphtheria	21
German measles	5
Influenza	2
Measles	38
Mumps	1
Pneumonia	5
Poliomyelitis	1
Scarlet fever	31
Smallpox	15
Tuberculosis	14
Typhoid fever	2
Whooping cough	114

Reports for Week Ended July 26, 1924.

DISTRICT OF COLUMBIA.	Cases.
Chicken pox	7
Diphtheria	2
Measles	2
Scarlet fever	4
Tuberculosis	32
Typhoid fever	1
Whooping cough	10

NEBRASKA.	
Chicken pox	2
Diphtheria	11
Measles	1
Scarlet fever	2
Septic sore throat	3
Smallpox	1
Tetanus	2
Typhoid fever	1
Whooping cough	6

NORTH DAKOTA.	
Diphtheria	5
Measles	18
Pneumonia	4
Scarlet fever	11
Smallpox	13
Trachoma	1
Tuberculosis	5
Typhoid fever	2
Whooping cough	4

[1] Deaths.

SUMMARY OF MONTHLY REPORTS FROM STATES.

The following summary of monthly State reports is published weekly and covers only those States from which reports are received during the current week.

State.	Cerebrospinal meningitis.	Diphtheria.	Influenza.	Malaria.	Measles.	Pellagra.	Poliomyelitis.	Scarlet fever.	Smallpox.	Typhoid fever.
May, 1924.										
California	5	954	82	18	3,067	5	1	755	961	63
June, 1924.										
Hawaii		10	16	5	35			2		11
New Jersey		279	21		1,834			512	57	36
New York	24	1,505	70	11	7,068		22	1,574	39	228
Virginia	6	61	312	309	870	10	3	51	43	128
Wyoming		2	1		56			10	5	3

TYPHUS FEVER—TEXAS.

Information received from Fort Ringgold, Tex., under date of July 30, 1924, reports new cases of typhus fever during the preceding week as follows: Donna, 1 case; Edinburg, 1 case; Fort Ringgold, 2 cases; Laredo, 1 case; Rio Grande City, 1 case. No deaths from the disease have been reported

GENERAL CURRENT SUMMARY AND WEEKLY REPORTS FROM CITIES.

Diphtheria.—For the week ended July 19, 1924, 33 States reported 1,052 cases of diphtheria. For the week ended July 21, 1923, the same States reported 1,056 cases of this disease. One hundred and two cities, situated in all parts of the country and having an aggregate population of more than 28,600,000, reported 646 cases of diphtheria for the week ended July 19, 1924. Last year for the corresponding week they reported 608 cases. The estimated expectancy for these cities was 631 cases. The estimated expectancy was based on the experience of the last nine years, excluding epidemics.

Measles.—Twenty-eight States reported 1,801 cases of measles for the week of this year and 3,947 cases for the week last year. One hundred and two cities reported 670 cases of measles for the week this year, and 1,105 cases last year.

Scarlet fever.—Scarlet fever was reported for the week as follows: Thirty-three States—this year, 924 cases; last year, 958 cases. One hundred and two cities—this year, 439 cases; last year, 358 cases; estimated expectancy, 281 cases.

Smallpox.—For the week ended July 19, 1924, 33 States reported 395 cases of smallpox. Last year for the corresponding week they reported 289 cases of this disease. One hundred and two cities reported smallpox for the week as follows: 1924, 158 cases; 1923, 79 cases; estimated expectancy, 62 cases.

Typhoid fever.—Six hundred and sixty-three cases of typhoid fever were reported for the week ended July 19, 1924, by 32 States. For the corresponding week of 1923 the number was 656 cases. One hundred and two cities reported 197 cases of typhoid fever for the week this year and 177 cases for the week last year. The estimated expectancy for these cities was 163 cases.

Influenza and pneumonia.—Deaths from influenza and pneumonia (combined) were reported for the week by 102 cities as follows: 1924, 310 deaths; 1923, 294 deaths.

City reports for week ended July 19, 1924.

The "estimated expectancy" given for diphtheria, poliomyelitis, scarlet fever, smallpox, and typhoid fever is the result of an attempt to ascertain from previous occurrence how many cases of the disease under consideration may be expected to occur during a certain week in the absence of epidemics. It is based on reports to the Public Health Service during the past nine years. It is in most instances the median number of cases reported in the corresponding week of the preceding years. When the reports include several epidemics, or when for other reasons the median is unsatisfactory, the epidemic periods are excluded and the estimated expectancy is the mean number of cases reported for the week during nonepidemic years.

If reports have not been received for the full nine years, data are used for as many years as possible, but no year earlier than 1915 is included. In obtaining the estimated expectancy, the figures are smoothed when necessary to avoid abrupt deviations from the usual trend. For some of the diseases given in the table the available data were not sufficient to make it practicable to compute the estimated expectancy.

Division, State, and city.	Chicken pox, cases reported.	Diphtheria.		Influenza.		Measles, cases reported.	Mumps, cases reported.	Pneumonia, deaths reported.	Scarlet fever.	
		Cases, estimated expectancy.	Cases reported.	Cases reported.	Deaths reported.				Cases, estimated expectancy.	Cases reported.
NEW ENGLAND.										
Maine:										
Lewiston	1	0	1	0	0	2	0	2	1	5
Portland	0	1	2	0	0	0	0	1	0	0
New Hampshire:										
Concord	0	1	0	0	0	1	0	0	0	0
Manchester	----	2	0	0	0	0	----	0	0	0
Vermont:										
Barre	0	0	0	0	0	0	0	0	0	0
Burlington	1	1	1	0	0	0	0	0	0	0
Massachusetts:										
Boston	14	39	37	0	0	22	10	5	14	19
Fall River	3	2	5	0	0	2	0	0	1	1
Springfield	2	1	3	0	0	3	3	0	2	2
Worcester	----	3	6	0	0	2	----	3	2	3
Rhode Island:										
Pawtucket	0	1	0	0	0	0	0	0	1	1
Providence	0	6	2	0	0	2	0	1	2	5
Connecticut:										
Bridgeport	1	4	9	0	0	0	0	1	2	1
Hartford	2	4	7	0	0	11	0	0	1	3
New Haven	0	2	0	0	0	9	0	3	1	4
MIDDLE ATLANTIC.										
New York:										
Buffalo	0	10	9	0	0	3	0	6	8	5
New York	55	157	179	5	0	121	36	76	43	45
Rochester	1	6	0	0	0	13	3	3	4	9
Syracuse	8	5	4	0	0	5	3	1	3	5
New Jersey:										
Camden	1	2	5	0	0	6	1	0	1	1
Newark	----	10	5	2	0	41	----	4	5	7
Trenton	3	3	5	0	1	1	1	0	0	0
Pennsylvania:										
Philadelphia	45	38	51	----	0	66	40	18	19	21
Pittsburgh	36	13	15	1	0	26	23	18	7	21
Reading	4	2	1	0	0	1	12	1	1	0
Scranton	1	2	1	0	0	1	0	1	1	1

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Chicken pox, cases reported.	Diphtheria.		Influenza.		Measles, cases reported	Mumps, cases reported.	Pneumonia, deaths reported.	Scarlet fever.	
		Cases, estimated expectancy.	Cases reported.	Cases reported	Deaths reported.				Cases, estimated expectancy.	Cases reported.
E. NORTH CENTRAL.										
Ohio:										
Cincinnati	0	7	7	0	0	5	0	4	4	6
Cleveland	62	18	8	0	0	58	28	7	9	9
Columbus	1	2	0	0	0	2	1	2	2	0
Toledo	13	5	1	0	0	11	0	2	8	2
Indiana:										
Fort Wayne	----	2	8	0	0	0	----	0	1	1
Indianapolis	2	5	0	0	0	5	7	4	4	1
South Bend	0	0	0	0	0	2	0	0	0	3
Terre Haute	0	0	0	0	0	0	0	0	1	0
Illinois:										
Chicago	55	77	62	3	0	89	25	24	28	42
Cicero	0	2	0	0	0	0	0	1	0	0
Springfield	----	0	2	0	0	0	----	0	0	0
Michigan:										
Detroit	21	35	16	0	1	14	7	9	24	29
Flint	0	5	0	0	0	2	2	0	1	0
Grand Rapids	10	3	6	0	0	3	1	2	2	6
Saginaw	2	1	0	0	0	0	0	0	1	1
Wisconsin:										
Madison	7	0	2	0	0	0	0	0	1	1
Milwaukee	47	9	6	0	0	18	5	0	14	2
Racine	11	1	3	0	0	4	0	0	1	1
Superior	1	1	0	0	0	0	0	0	1	1
W. NORTH CENTRAL.										
Minnesota:										
Duluth	2	1	0	0	0	4	0	0	1	16
Minneapolis	31	9	7	0	0	5	1	3	7	16
St. Paul	----	10	10	0	0	2	----	3	4	9
Iowa:										
Sioux City	0	1	0	0	----	0	0	----	1	0
Waterloo	3	0	0	0	----	1	1	----	1	1
Missouri:										
Kansas City	2	3	2	0	0	2	4	4	2	3
St. Joseph	1	1	0	0	0	2	0	0	0	0
St. Louis	5	23	14	0	0	16	13	0	6	43
North Dakota:										
Fargo	1	0	0	0	1	0	0	----	0	1
Grand Forks	0	1	0	0	0	0	0	0	0	1
South Dakota:										
Aberdeen	0	0	0	0	0	1	0	0	1	0
Sioux Falls	0	0	0	0	0	0	1	0	1	0
Nebraska:										
Lincoln	----	0	2	0	0	0	----	0	0	0
Omaha	0	4	2	0	0	0	0	3	2	1
Kansas:										
Topeka	0	1	1	0	0	1	7	0	1	1
Wichita	0	1	0	0	0	2	0	4	1	1
SOUTH ATLANTIC.										
Delaware:										
Wilmington	----	1	----	----	----	----	----	----	1	----
Maryland:										
Baltimore	14	11	10	5	0	32	9	12	6	11
Cumberland	----	1	1	0	1	0	----	0	1	0
Frederick	0	0	0	0	0	0	0	0	0	0
District of Columbia:										
Washington	4	4	4	1	0	1	----	8	3	12
Virginia:										
Lynchburg	0	1	0	0	0	0	1	0	0	0
Norfolk	0	1	0	0	0	1	6	1	1	0
Richmond	0	1	5	0	0	8	0	7	1	3
Roanoke	0	1	0	0	0	1	0	0	0	1
West Virginia:										
Charleston	0	1	0	0	0	3	0	0	0	0
Huntington	0	1	0	0	0	0	0	1	1	0
Wheeling	1	0	1	0	0	1	1	1	1	1
North Carolina:										
Raleigh	0	0	1	0	0	3	0	0	0	1
Wilmington	----	0	0	0	0	1	----	0	0	0
Winston-Salem	2	1	1	0	0	1	3	1	1	2

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Chicken pox, cases reported.	Diphtheria.		Influenza.		Measles, cases reported.	Mumps, cases reported.	Pneumonia, deaths reported.	Scarlet fever.	
		Cases, estimated expectancy.	Cases reported.	Cases reported.	Deaths reported.				Cases, estimated expectancy.	Cases reported.
SOUTH ATLANTIC—continued.										
South Carolina:										
Charleston	0	0	0	0	0	0	0	1	0	1
Columbia	0	1	0	0	0	2	1	0	0	0
Greenville	0	1	0	0	0	0	0	0	0	0
Georgia:										
Atlanta	0	3	0	1	0	0	0	4	2	0
Brunswick	0	0	0	0	0	0	1	0	0	0
Savannah	0	1	1	0	0	1	0	0	0	0
Florida:										
St. Petersburg	0	0	0	0	0	0	0	0	0	0
Tampa	----	0	1	1	0	0	----	1	0	0
EAST SOUTH CENTRAL.										
Kentucky:										
Covington	0	1	0	0	0	1	0	0	0	0
Lexington	0	1	1	0	0	2	0	1	0	0
Louisville	1	2	0	0	0	4	3	2	1	0
Tennessee:										
Memphis	0	2	0	0	0	0	0	5	0	4
Nashville	----	1	1	0	0	1	----	3	0	1
Alabama:										
Birmingham	----	1	1	0	0	0	----	2	1	0
Mobile	0	0	0	0	0	3	0	0	0	2
Montgomery	0	1	0	0	0	4	1	0	1	0
WEST SOUTH CENTRAL.										
Arkansas:										
Fort Smith	----	0	----	----	----	----	----	----	1	----
Little Rock	0	0	0	0	0	0	0	2	1	0
Louisiana:										
New Orleans	0	5	2	0	0	1	0	9	0	1
Shreveport	0	----	0	0	0	0	0	1	----	0
Oklahoma:										
Oklahoma	0	0	0	0	0	0	0	1	1	0
Texas:										
Dallas	0	2	1	0	0	2	1	1	1	3
Galveston	0	1	0	0	0	0	0	1	0	0
Houston	----	2	0	0	0	0	----	3	0	0
San Antonio	0	1	2	0	0	0	0	5	0	0
MOUNTAIN.										
Montana:										
Billings	3	0	0	0	0	0	0	0	0	0
Great Falls	0	1	1	0	0	0	0	0	0	1
Helena	0	1	0	0	0	0	0	1	0	0
Missoula	0	0	0	0	0	0	0	0	0	0
Idaho:										
Boise	1	0	0	0	0	3	0	0	1	0
Colorado:										
Denver	7	6	19	0	0	1	5	1	4	6
Pueblo	----	2	0	0	0	0	----	0	0	4
New Mexico:										
Albuquerque	----	2	1	0	0	0	----	0	0	0
Utah:										
Salt Lake City	13	2	5	0	0	3	6	2	2	3
Nevada:										
Reno	0	0	0	0	0	0	0	0	0	0
PACIFIC.										
Washington:										
Seattle	24	4	2	0	----	1	1	----	3	5
Spokane	0	1	0	0	----	0	0	----	1	0
Tacoma	0	1	2	0	----	1	0	----	1	2
Oregon:										
Portland	5	4	11	0	0	2	3	3	3	4
California:										
Los Angeles	31	25	55	1	1	20	3	13	5	16
Sacramento	2	1	14	0	0	3	0	0	1	1
San Francisco	9	10	20	2	0	1	0	8	5	10

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Population July 1, 1923, estimated.	Smallpox.			Tuberculosis, deaths reported.	Typhoid fever.			Whooping cough, cases reported.	Deaths, all causes.
		Cases, estimated expectancy.	Cases reported.	Deaths reported.		Cases, estimated expectancy.	Cases reported.	Deaths reported.		
NEW ENGLAND.										
Maine:										
Lewiston	33,790	0	0	0	0	0	0	0	0	11
Portland	73,129	0	0	0	2	0	1	1	5	19
New Hampshire:										
Concord	22,408	0	0	0	0	0	0	0	0	5
Manchester	81,383	0	0	0	1	0	0	0	------	20
Vermont:										
Barre	*10,008	0	0	0	0	0	0	0	0	0
Burlington	23,613	0	0	0	0	0	0	0	1	6
Massachusetts:										
Boston	770,400	0	0	0	17	3	2	0	17	173
Fall River	120,912	0	0	0	1	1	1	0	5	21
Springfield	144,227	0	0	0	1	0	0	0	2	23
Worcester	191,927	0	0	0	1	0	0	0	------	44
Rhode Island;										
Pawtucket	68,709	0	0	0	0	0	0	0	0	19
Providence	242,378	0	0	0	1	0	2	0	0	45
Connecticut:										
Bridgeport	*143,555	0	0	0	2	0	0	0	1	18
Hartford	*138,036	0	0	0	4	1	1	0	5	34
New Haven	172,967	0	0	0	0	2	0	0	10	37
MIDDLE ATLANTIC.										
New York:										
Buffalo	536,718	1	0	0	5	2	0	0	35	87
New York	5,927,625	1	0	0	[1]105	20	39	5	217	1,164
Rochester	317,867	0	0	0	2	1	0	0	4	44
Syracuse	184,511	0	0	0	1	1	0	0	5	31
New Jersey:										
Camden	124,157	0	0	0	0	1	0	0	6	20
Newark	438,699	0	0	0	7	1	2	0	------	92
Trenton	127,390	0	4	0	2	1	1	0	7	43
Pennsylvania:										
Philadelphia	1,922,788	1	0	0	38	10	7	0	104	402
Pittsburgh	613,442	0	12	4	9	4	1	0	47	123
Reading	110,917	0	1	0	2	1	0	0	20	33
Scranton	140,636	0	0	0	1	0	0	0	1	------
EAST NORTH CENTRAL.										
Ohio:										
Cincinnati	406,312	1	6	0	15	2	3	0	8	102
Cleveland	888,519	2	4	0	15	3	1	0	76	158
Columbus	261,082	0	0	0	7	1	1	0	1	65
Toledo	268,338	1	19	1	3	1	1	0	57	42
Indiana:										
Fort Wayne	93,573	0	0	0	1	1	1	0	------	13
Indianapolis	342,718	1	7	0	5	2	4	1	38	92
South Bend	76,709	1	0	0	0	0	1	0	0	10
Terre Haute	68,939	0	0	0	1	0	1	1	0	24
Illinois:										
Chicago	2,886,121	1	12	0	56	3	4	3	94	511
Cicero	55,968	0	0	0	1	0	0	0	1	8
Springfield	61,833	1	0	0	0	1	0	0	------	21
Michigan:										
Detroit	995,668	3	10	0	24	6	1	0	102	199
Flint	117,968	1	1	0	2	1	0	0	0	20
Grand Rapids	145,947	0	1	0	1	0	1	0	4	29
Saginaw	69,754	0	0	0	2	1	1	0	0	16
Wisconsin:										
Madison	42,519	0	0	0	0	0	0	0	13	------
Milwaukee	484,595	2	1	0	0	1	2	1	33	75
Racine	64,393	1	1	0	0	0	0	0	1	5
Superior	*39,671	2	1	0	1	1	0	0	0	12

* Population Jan. 1, 1920.
[1] Pulmonary only.

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Population July 1, 1923, estimated.	Smallpox.			Tuberculosis, deaths reported.	Typhoid fever.			Whooping cough, cases reported.	Deaths, all causes.
		Cases, estimated expectancy.	Cases reported.	Deaths reported.		Cases, estimated expectancy.	Cases reported.	Deaths reported.		
WEST NORTH CENTRAL.										
Minnesota:										
Duluth	106,289	1	6	2	0	1	0	0	4	12
Minneapolis	409,125	4	15	5	8	1	0	0	5	75
St. Paul	241,891	3	7	0	7	1	2	1	----	50
Iowa:										
Sioux City	79,662	0	0	----	----	0	0	----	0	----
Waterloo	39,667	1	0	----	----	0	0	----	3	----
Missouri:										
Kansas City	351,819	1	0	0	9	2	0	0	8	98
St. Joseph	78,232	0	0	0	1	1	0	0	0	33
St. Louis	803,853	1	0	0	8	7	6	1	6	184
North Dakota:										
Fargo	24,841	0	0	0	0	0	0	0	0	4
Grand Forks	14,547	1	0	0	0	0	0	0	0	----
South Dakota:										
Aberdeen	15,829	----	0	0	0	0	0	0	1	----
Sioux Falls	29,206	0	0	0	0	0	0	0	1	3
Nebraska:										
Lincoln	58,761	1	0	0	0	1	0	0	----	7
Omaha	204,382	2	5	0	3	0	2	0	0	52
Kansas:										
Topeka	52,555	1	0	0	0	0	0	0	11	12
Wichita	79,261	1	0	0	0	1	0	0	1	17
SOUTH ATLANTIC.										
Delaware:										
Wilmington	117,728	0	----	----	----	1	----	----	----	----
Maryland:										
Baltimore	773,580	0	0	0	24	8	5	0	41	186
Cumberland	32,361	0	0	0	1	0	0	0	----	7
Frederick	11,301	0	0	0	0	0	1	0	0	2
District of Columbia:										
Washington	*437,571	1	0	0	8	5	1	0	4	116
Virginia:										
Lynchburg	30,277	0	0	0	0	1	1	0	0	7
Norfolk	159,089	0	0	0	2	3	1	1	5	----
Richmond	181,044	0	0	0	7	2	3	0	5	69
Roanoke	55,502	0	0	0	0	1	2	0	0	11
West Virginia:										
Charleston	45,597	0	0	0	0	2	1	1	2	10
Huntington	57,918	0	1	0	1	1	2	0	0	16
Wheeling	*56,208	0	0	0	1	0	0	0	0	13
North Carolina:										
Raleigh	29,171	0	1	0	1	0	1	0	0	10
Wilmington	35,719	0	0	0	1	1	0	0	----	6
Winston-Salem	56,230	1	1	0	5	2	2	0	2	32
South Carolina:										
Charleston	71,245	0	0	0	2	2	1	2	1	30
Columbia	39,688	0	0	0	1	1	2	1	1	25
Greenville	25,789	0	2	0	0	1	3	0	4	3
Georgia:										
Atlanta	222,963	3	1	0	1	2	9	2	3	61
Brunswick	15,937	0	0	0	0	1	0	0	0	5
Savannah	89,448	0	0	0	4	2	2	1	0	32
Florida:										
St. Petersburg	24,403	0	0	0	0	0	0	0	0	8
Tampa	56,050	0	0	0	0	0	1	0	----	11
EAST SOUTH CENTRAL.										
Kentucky:										
Covington	57,877	1	0	0	1	1	0	0	0	20
Lexington	43,673	0	1	0	1	1	0	0	0	19
Louisville	257,671	0	3	0	5	6	2	0	5	74
Tennessee:										
Memphis	170,067	1	0	0	9	4	13	6	0	73
Nashville	121,128	0	2	0	3	5	3	0	----	39
Alabama:										
Birmingham	195,901	1	12	0	12	4	2	0	----	71
Mobile	63,858	1	0	0	2	1	4	1	0	23
Montgomery	45,383	0	1	0	1	1	7	1	0	----

* Population Jan. 1, 1920.

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Population, July 1, 1923, estimated.	Smallpox.			Tuberculosis, deaths reported.	Typhoid fever.			Whooping cough, cases reported.	Deaths, all causes.
		Cases, estimated expectancy.	Cases reported.	Deaths reported.		Cases, estimated expectancy.	Cases reported.	Deaths reported.		
WEST SOUTH CENTRAL.										
Arkansas:										
Fort Smith	30,635	0	------	------	------	0	------	------	------	------
Little Rock	70,916	0	0	0	2	2	19	2	0	------
Louisiana:										
New Orleans	404,575	1	0	0	12	4	2	0	4	143
Shreveport	54,590	0	0	0	1	0	0	0	0	32
Oklahoma:										
Oklahoma	101,150	1	1	0	0	2	6	0	0	30
Texas:										
Dallas	177,274	1	0	0	5	3	5	0	22	55
Galveston	46,877	0	0	0	2	1	0	0	0	14
Houston	154,970	0	0	0	5	1	0	1	------	58
San Antonio	184,727	0	0	0	4	------	0	0	0	44
MOUNTAIN.										
Montana:										
Billings	16,927	0	0	0	0	0	0	0	0	4
Great Falls	27,787	0	1	0	0	0	0	0	0	6
Helena	*12,037	0	0	0	0	0	0	0	0	6
Missoula	*12,668	1	1	0	0	0	0	0	0	6
Idaho:										
Boise	22,806	1	1	0	0	0	0	0	0	1
Colorado:										
Denver	272,031	3	0	0	6	2	0	1	23	69
Pueblo	43,519	0	0	0	1	1	0	1	------	9
New Mexico:										
Albuquerque	16,648	0	0	0	5	0	0	0	------	14
Utah:										
Salt Lake City	126,241	2	1	0	3	1	4	0	4	27
Nevada:										
Reno	12,429	0	0	0	0	0	0	0	0	6
PACIFIC.										
Washington:										
Seattle	*315,685	2	1	------	------	0	0	------	8	------
Spokane	104,573	4	0	------	------	1	0	------	0	------
Tacoma	101,731	1	0	------	------	0	2	------	0	------
Oregon:										
Portland	273,621	3	20	0	2	0	0	0	2	48
California:										
Los Angeles	666,853	1	34	0	29	4	7	0	25	206
Sacramento	69,950	0	2	0	0	1	3	0	0	13
San Francisco	539,038	1	0	0	5	1	1	0	2	138

* Population Jan. 1, 1920.

Division, State, and city.	Cerebro-spinal meningitis.		Dengue.		Lethargic encephalitis.		Pellagra.		Poliomyelitis (infantile paralysis).			Typhus fever.	
	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases, est. expectancy.	Cases.	Deaths.	Cases.	Deaths.
NEW ENGLAND.													
Massachusetts:													
Boston	2	1	0	0	0	0	3	1	0	3	0	0	0
Connecticut:													
Bridgeport	1	0	0	0	1	1	0	0	0	0	0	0	0
Hartford	1	0	0	0	1	0	0	0	0	1	0	0	0

City reports for week ended July 19, 1924—Continued.

Division, State, and city.	Cerebrospinal meningitis.		Dengue.		Lethargic encephalitis.		Pellagra.		Poliomyelitis (infantile paralysis).			Typhus fever.	
	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases, est. expectancy.	Cases.	Deaths.	Cases.	Deaths.
MIDDLE ATLANTIC.													
New York:													
New York	7	3	0	0	2	4	1	0	4	1	0	1	0
Syracuse	0	0	0	0	0	0	0	0	0	3	0	0	0
New Jersey:													
Newark	1	0	0	0	0	0	0	0	0	0	0	0	0
Pennsylvania:													
Philadelphia	0	1	0	0	0	0	0	0	1	1	0	0	0
Pittsburgh	0	1	0	0	0	0	0	0	1	0	0	0	0
EAST NORTH CENTRAL.													
Ohio:													
Cleveland	0	1	0	0	0	0	0	0	1	0	1	0	0
Illinois:													
Chicago	0	0	0	0	1	0	0	0	2	1	0	0	0
WEST NORTH CENTRAL.													
Michigan:													
Detroit	3	0	0	0	1	0	0	1	1	1	1	0	0
Flint	0	1	0	0	0	1	0	0	0	0	0	0	0
SOUTH ATLANTIC.													
Maryland:													
Baltimore	0	0	0	0	0	0	0	1	1	0	0	0	0
Virginia:													
Richmond	0	1	0	0	0	0	0	0	0	0	0	0	0
West Virginia:													
Huntington	0	1	0	0	0	0	0	0	0	0	0	0	0
Wheeling	0	1	0	0	0	0	0	0	0	0	0	0	0
North Carolina:													
Winston-Salem	0	0	0	0	0	0	0	1	0	0	0	0	0
South Carolina:													
Charleston	0	0	0	0	0	0	0	2	0	0	0	0	0
Columbia	0	0	0	0	0	0	0	2	0	0	0	0	0
Georgia:													
Savannah	0	0	0	0	0	0	1	0	0	0	0	0	0
Florida:													
St. Petersburg	0	0	2	0	0	0	0	1	----	0	0	0	0
Tampa	0	0	0	0	0	0	1	0	0	0	0	0	0
EAST SOUTH CENTRAL.													
Tennessee:													
Memphis	0	0	0	0	0	0	0	1	0	0	0	0	0
Alabama:													
Birmingham	0	0	0	0	0	0	1	0	0	1	0	0	0
Mobile	0	0	0	0	0	0	0	1	----	0	0	0	0
WEST SOUTH CENTRAL.													
Louisiana:													
New Orleans	0	0	0	0	0	0	1	0	0	0	0	0	0
Shreveport	0	0	0	0	0	0	0	1	----	0	0	0	0
Texas:													
Dallas	0	0	0	0	0	0	0	1	0	0	0	0	0
San Antonio	0	0	0	0	0	0	0	1	----	0	0	0	0
MOUNTAIN.													
Utah:													
Salt Lake City	1	1	0	0	0	0	0	0	0	0	0	0	0
PACIFIC.													
California:													
Los Angeles	0	0	0	0	0	0	0	0	0	1	0	0	0

The following table gives a summary of the reports from 105 cities for the 10-week period ended July 19, 1924. The cities included in this table are those whose reports have been published for all 10 weeks in the Public Health Reports. Eight of these cities did not report deaths. The aggregate population of the cities reporting cases was estimated at nearly 29,000,000 on July 1, 1923, which is the latest date for which estimates are available. The cities reporting deaths had more than 28,000,000 population on that date. The number of cities included in each group and the aggregate population are shown in a separate table below.

Summary of weekly reports from cities, May 11 to July 19, 1924.

DIPHTHERIA CASES.

	1924, week ended—									
	May 17.	May 24.	May 31.	June 7.	June 14.	June 21.[1]	June 28.	July 5.	July 12.	July 19.
Total	930	927	868	919	911	885	878	666	689	652
New England	78	94	85	90	73	97	78	64	55	71
Middle Atlantic	357	340	371	387	405	368	387	296	301	274
East North Central	168	175	129	150	157	135	136	[2] 101	[3] 131	120
West North Central	110	106	80	76	55	65	36	50	52	36
South Atlantic	42	32	33	41	35	31	20	[4] 17	19	[5] 26
East South Central	3	8	4	8	6	4	8	1	3	2
West South Central	16	18	18	18	17	16	15	19	5	[6] 5
Mountain	18	30	14	37	15	30	30	19	36	25
Pacific	138	124	134	112	148	139	[7] 168	99	87	93

MEASLES CASES.

Total	4,019	3,716	2,942	3,240	2,847	2,302	1,857	1,188	987	676
New England	271	310	227	247	175	168	120	90	66	52
Middle Atlantic	1,868	1,571	1,231	1,483	1,287	1,051	774	535	422	283
East North Central	781	873	732	747	756	568	565	[2] 288	[3] 295	202
West North Central	197	128	124	130	97	87	63	46	29	35
South Atlantic	465	468	344	317	317	220	187	[4] 143	91	[5] 55
East South Central	56	56	47	36	32	26	19	15	15	13
West South Central	51	33	28	19	11	2	5	1	7	[6] 3
Mountain	100	79	70	50	20	33	35	22	11	7
Pacific	230	198	130	211	152	147	[7] 89	48	51	26

SCARLET FEVER CASES.

Total	1,503	1,311	1,208	1,243	1,067	973	717	563	559	441
New England	213	165	108	181	143	111	92	59	50	39
Middle Atlantic	452	406	380	401	335	331	226	186	144	114
East North Central	336	279	254	243	252	238	161	[2] 132	[3] 166	102
West North Central	223	182	167	182	160	128	102	68	100	93
South Atlantic	118	134	112	120	91	63	43	[4] 30	47	[5] 33
East South Central	9	9	8	11	6	6	1	1	7	7
West South Central	14	14	11	11	12	9	7	11	8	[6] 5
Mountain	25	30	17	17	3	13	12	16	4	14
Pacific	113	92	91	77	65	74	[7] 73	60	33	34

SMALLPOX CASES.

Total	529	408	327	472	334	346	238	159	169	158
New England	0	0	0	0	0	0	0	0	1	0
Middle Atlantic	5	1	1	8	7	10	16	19	16	17
East North Central	213	181	145	174	157	121	61	[2] 44	[3] 33	44
West North Central	39	26	19	40	33	34	41	23	47	33
South Atlantic	51	54	29	39	44	35	12	[4] 9	3	[5] 5
East South Central	54	33	36	107	22	65	36	23	21	18
West South Central	7	6	7	5	7	8	7	1	1	[6] 0
Mountain	6	3	7	2	6	10	9	5	6	4
Pacific	154	104	83	97	58	63	[7] 56	35	41	37

[1] Corrected figures.
[2] Figures for Racine, Wis., estimated. Report not received at time of going to press.
[3] Figures for Cicero, Ill., estimated.
[4] Figures for Frederick, Md., estimated.
[5] Figures for Wilmington, Del., estimated.
[6] Figures for Fort Smith, Ark., estimated.
[7] Figures for San Francisco, Calif., estimated.

Summary of weekly reports from cities, May 11 to July 19, 1924—Continued.

TYPHOID FEVER CASES.

	1924, week ended—									
	May 17.	May 24.	May 31.	June 7.	June 14.	June 21.[1]	June 28.	July 5.	July 12.	July 19.
Total	73	78	78	92	107	132	89	128	142	197
New England	2	6	9	3	7	8	4	2	6	7
Middle Atlantic	32	24	18	30	46	58	41	46	34	50
East North Central	12	7	6	11	9	11	11	[2] 9	[3] 20	20
West North Central	3	8	5	8	5	4	5	15	12	10
South Atlantic	8	18	13	12	10	16	10	[4] 23	25	[5] 36
East South Central	7	6	11	7	8	13	3	8	10	31
West South Central	3	5	10	13	13	8	4	8	21	[6] 26
Mountain	0	2	1	0	0	4	3	6	5	4
Pacific	6	2	5	8	9	10	[7] 8	11	9	13

INFLUENZA DEATHS.

Total	49	40	30	21	15	22	13	9	11	5
New England	1	2	1	1	1	0	1	1	0	0
Middle Atlantic	25	10	10	5	6	8	3	2	5	1
East North Central	5	11	10	3	2	2	3	[2] 2	[3] 1	1
West North Central	4	3	1	2	2	1	0	0	0	1
South Atlantic	5	6	5	3	1	5	4	[4] 3	2	1
East South Central	4	3	1	2	3	3	2	1	3	0
West South Central	3	1	1	2	0	3	0	0	0	0
Mountain	1	1	0	0	0	0	0	0	0	0
Pacific	1	3	1	3	0	0	[7] 0	0	0	1

PNEUMONIA DEATHS.

Total	743	644	630	590	573	521	434	358	319	307
New England	52	36	34	37	46	28	22	19	16	14
Middle Atlantic	343	285	267	276	250	214	200	167	141	127
East North Central	139	136	131	118	108	130	91	[2] 62	[3] 56	53
West North Central	41	38	40	22	40	34	11	15	22	17
South Atlantic	86	64	60	66	51	50	50	[4] 39	39	[5] 37
East South Central	22	32	40	18	20	12	15	14	9	12
West South Central	27	27	14	18	27	24	12	16	16	22
Mountain	13	11	18	14	15	9	12	8	10	4
Pacific	20	15	26	21	16	20	[7] 21	18	10	21

Number of cities included in summary of weekly reports and aggregate population of cities in each group, estimated as of July 1, 1923.

Group of cities.	Number of cities reporting cases.	Number of cities reporting deaths.	Aggregate population of cities reporting cases.	Aggregate population of cities reporting deaths.
Total	105	97	28,898,350	28,140,934
New England	12	12	2,098,746	2,098,746
Middle Atlantic	10	10	10,304,114	10,304,114
East North Central	17	17	7,032,535	7,032,535
West North Central	14	11	2,515,330	2,381,454
South Atlantic	22	22	2,566,901	2,566,901
East South Central	7	7	911,885	911,885
West South Central	8	6	1,124,564	1,023,013
Mountain	9	9	546,445	546,445
Pacific	6	3	1,797,830	1,275,841

[1] Corrected figures.
[2] Figures for Racine, Wis., estimated. Report not received at time of going to press.
[3] Figures for Cicero, Ill., estimated.
[4] Figures for Frederick, Md., estimated.
[5] Figures for Wilmington, Del., estimated.
[6] Figures for Fort Smith, Ark., estimated.
[7] Figures for San Francisco, Calif., estimated.

FOREIGN AND INSULAR.

BRAZIL.

Leprosy—State of Amazonas—Manaos.

In a report dated May 31, 1924, addressed by the Federal and State health departments to the governor of Amazonas, Brazil, attention is called to the spread of leprosy in the State, and especially in the city of Manaos, the number of registered cases in the city being stated at 520 as compared with 440 cases registered in September, 1923. Of the 520 cases present in May, 1924, only 70 were reported as isolated in the leper colony at Umirisal, which is situated in the vicinity of the city. It was estimated that the number of cases not registered was about 30 per cent of the registered cases. The facilities at the leper colony for the reception and care of lepers were stated to be inadequate. [1]

Leprosy—State of Ceara.

Information received under date of June 11, 1924, in regard to a recent inspection made by the leper service of conditions existing in the northern section of the State of Ceara, Brazil, shows that 77 lepers were recognized, of whom 71 were in a stage of the disease requiring isolation. The lepers were found in 19 localities. A few of the cases observed were stated to be isolated. The greater number lived with their families. At Sobral, where in 1912 there were known to be 4 lepers, there were in June, 1924, 29 lepers. Of this number 11 were stated to have received treatment with chaulmoogra oil. All but one were stated to be improved.

COLOMBIA.

Sanitary Conditions—Buenaventura.

Information dated June 8, 1924, regarding sanitary conditions at Buenaventura, Republic of Colombia, shows the existence of a sanitary corps consisting of a chief inspector, 4 inspectors, and 23 laborers, paid by the Colombian government. The inspectors are empowered to make arrests; and, in case of violation of sanitary regulations, fines are imposed by the municipality. Metal cans with covers are provided for the collection of garbage, which is dumped into the ocean. Storage tanks for rain water, which is the only water supply of the town, are required to be covered. Spraying with oil to prevent breeding of mosquitoes is carried out. There were stated to be few mosquitoes or house flies in Buenaventura. For the 32 weeks preceding June 8, mortality reports were stated to show 96 deaths, equivalent to an annual death rate of 39 per 1,000 inhabitants.

[1] Public Health Reports, Nov. 2, 1923, p. 2649.

COSTA RICA.

Mosquito Control—Sanitary Conditions—Port Limon.

Information dated June 28, 1924, in regard to mosquito control at Port Limon, Costa Rica, shows that sanitary inspectors are employed to see that all water tanks and other permanent receptacles of water are properly screened and that no tins or bottles capable of retaining water in which mosquitoes could breed are allowed to accumulate; all ditches and open drains are kept open and flowing if possible; larvæ-consuming small fish have also been introduced into ditches and drains and appear to be sufficiently effective to render oiling unnecessary. In some places, chemical means are employed to destroy larvæ. Port Limon was stated to be remarkably free from mosquitoes. Fly conditions were stated to be equally satisfactory. The national public health service in 1921 established a service for hookworm control and for venereal disease prophylaxis, but no activities in either branch have been reported. Milk supply was stated to be tested at irregular intervals for impurity or adulteration. No milk is pasteurized. Dairy inspection is also performed. Provision stores, cantinas, and hotels and restaurants are subject to inspection as regards sanitary condition of food and premises and health of personnel. Vaccination of school children is required and is carried out by the municipal physician. Children are not excluded from school for illness.

Percentage of Total Mortality for Certain Diseases—Port Limon.

Disease.	1920.	1921.	1922.	Disease.	1920.	1921.	1922.
Tuberculosis	12.5	14.05	6.96	Organic diseases of the heart		6.43	7.59
Pneumonia	18.5	9.35	10.42	Malarial fever	15.5	15.20	16.45
Influenza	5.3			All other	39.9	42.69	45.59
Nephritis	8.3	12.28	13.29				

CUBA.

Communicable Diseases—Habana.

Communicable diseases have been notified at Habana as follows:

Disease.	July 11–20, 1924.		Remaining under treatment July 20, 1924.	Disease.	July 11–20, 1924.		Remaining under treatment July 20, 1924.
	New cases.	Deaths.			New cases.	Deaths.	
Diphtheria	5	1	5	Paratyphoid fever			11
Leprosy			15	Scarlet fever			3
Malaria	21	3	[1] 45	Typhoid fever	100	20	[2] 366
Measles	3		5				

[1] From the interior, 18.

[2] From the interior, 28.

Typhoid Fever Decrease.

During the period under report, typhoid fever occurrence at Habana showed a decided decrease from the reported occurrence for the period July 1 to 10, 1924, viz, 100 cases with 20 deaths, as compared with 204 cases with 39 deaths.

Typhoid Fever—Santiago.[1]

During the week ended July 19, 1924, 13 cases of typhoid fever with three deaths were reported at Santiago, Cuba. It was stated that a large number of unreported cases of typhoid fever were believed to exist in the city.

EGYPT.

Status of Plague.

During the week ended June 24, 1924, 15 cases of plague, occurring in six districts, were reported in Egypt. From January 1 to June 24, 1924, the total of reported cases of plague in Egypt was 313, as compared with 1,069 cases occurring during the corresponding period in 1923.

ESTHONIA.

Communicable Diseases—May, 1924.

During the month of May, 1924, communicable diseases were reported in the Republic of Esthonia as follows:

Disease.	Cases.	Disease.	Cases.
Diphtheria	36	Tuberculosis	207
Measles	55	Typhoid fever	69
Scarlet fever	45	Typhus fever	9

ITALY.

Kala-azar—Malta Fever—Catania.

During the week ended June 29, 1924, a case of kala-azar and a case of Malta fever were reported in the city of Catania, Italy.

Chicken Pox—Catania Province.

During the two weeks ended June 29, 1924, three cases of chicken pox, of which one case was stated to be malignant pustular varicella, were reported in the Province of Catania, Italy.

JAMAICA.

Smallpox (Reported as Alastrim).

During the week ended July 12, 1924, 7 new cases of smallpox (reported as alastrim) were reported in the island of Jamaica. Of these, 2 cases were reported in the parish of Kingston.

[1] Public Health Reports, July 11, 1924, p. 1717, and Aug. 1, 1924, p. 1923

Chicken Pox.

During the same period, 2 new cases of chicken pox were reported in the island.

LATVIA.

Communicable Diseases—Month of May, 1924.

During the month of May, 1924, communicable diseases were reported in the Republic of Latvia as follows:

Disease.	Cases.	Disease.	Cases.
Cerebrospinal meningitis	3	Smallpox	1
Diphtheria	41	Typhoid fever	70
Measles	191	Typhus fever	43
Scarlet fever	85	Whooping cough	41

Population, estimated, 1,900,000.

Influenza—Leprosy—Tetanus.

During the period under report, 12 cases of influenza, one case of leprosy, and one of tetanus, were reported in the Republic of Latvia.

MEXICO.

Ordinance Relative to Persons Handling Foodstuffs—Nogales.

According to information dated July 10, 1924, the Legislature of the State of Sonora, Mexico, has approved an ordinance passed by the municipal government of the town of Nogales, Mexico, relative to persons handling food stuffs in the municipality.

From the day of publication in the Official Bulletin (June 7, 1924), the ordinance forbids all persons suffering from a contagious disease to engage in the business of dealing in food stuffs. All persons working in bakeries, restaurants, and hotels, are required to obtain a medical certificate from the municipal physician stating that the person is in good health, which certificate, with a photograph of the bearer attached, must be posted in a conspicuous place in the establishment in which he works. The certificate must be registered with the secretary of the municipality, and certificates and registrations must be secured within ten days following the publication of the ordinance. The medical certificate is valid two months only and must be renewed before its termination. Infraction of the ordinance is punishable with fine.

Tuberculosis—Vera Cruz—1901–1923.

Information dated July 19, 1924, shows mortality from tuberculosis during the period 1901–1923, inclusive, at Vera Cruz, Mexico, with the greatest number of deaths, viz, 428, occurring in the years 1906 and 1908, and a total number of tuberculosis deaths for the period

under report, of 7,913. The lowest number of deaths reported was for the year 1923, viz, 221. The population, November, 1922, was said to be 57,000. It was stated that no effort was being made to check the spread of the disease.

Year.	Deaths.	Year.	Deaths.	Year.	Deaths.	Year.	Deaths.
1901	337	1907	409	1913	330	1919	352
1902	362	1908	428	1914	272	1920	341
1903	363	1909	362	1915	355	1921	327
1904	328	1910	335	1916	360	1922	345
1905	399	1911	374	1917	255	1923	221
1906	428	1912	311	1918	319		

PANAMA CANAL.

Communicable Diseases—June, 1924.

During the month of June, 1924, communicable diseases were reported in the Panama Canal Zone, Colon, and Panama as follows:

Disease.	Canal Zone.	Colon.	Panama.	Nonresident.	Total.
Chicken pox	4	1	6		11
Diphtheria			10		10
Dysentery			1	4	5
Hookworm disease	15	13	43	47	118
Leprosy	1			2	3
Malaria	211	3	10	32	256
Measles	20	21	2	2	45
Mumps	3			2	5
Paratyphoid fever			1		1
Pneumonia	1	5	22		28
Poliomyelitis			1		1
Tuberculosis	7	3	19	6	35
Typhoid fever				1	1
Whooping cough	17	10			27

PERSIA.

Plague—Month of May, 1924.

During the month of May, 1924, plague was reported in Persia as follows: Abadan, cases, 20; deaths, 12; Bandar Abbas, cases, 11; deaths, 6; Bushire, one case landed at quarantine; Mohammerah, cases, 111; deaths, 78.

VIRGIN ISLANDS.

Communicable Diseases—June, 1924.

During the month of June, 1924, communicable diseases were reported in the Virgin Islands of the United States as follows:

Island and disease.	Cases.	Remarks.	Island and disease.	Cases.	Remarks.
St. Thomas and St. John:			St. Croix—Contd.		
Chancroid	2		Dysentery	2	Entamebic, 1; unclassified, 1.
Gonorrhea	2		Filariasis	5	Bancrofti.
Pellagra	1		Gonorrhea	1	
Syphilis	1	Secondary.	Syphilis	6	Secondary.
Tuberculosis	2	Chronic pulmonary.	Trachoma	9	
St. Croix:			Tuberculosis	1	Chronic pulmonary.
Chancroid	3				

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER.

The reports contained in the following tables must not be considered as complete or final as regards either the lists of countries included or the figures for the particular countries for which reports are given.

Reports Received During Week Ended August 8, 1924.[1]

CHOLERA.

Place.	Date.	Cases.	Deaths.	Remarks.
India:				
Rangoon	June 15-21	13	11	
Indo-China:				
Saigon	June 1-7	2	2	Including 100 square kilometers of surrounding country.
Siam:				
Bangkok	June 8-14	4	3	

PLAGUE.

British East Africa:				
Kenya—				
Tanganyika Territory	June 1-7	1	1	
China:				
Amoy	June 15-21		1	
Foochow	June 15-21		1	Number of cases not reported.
Egypt				June 18-24, 1924: Cases 15. In 6 districts. Total, Jan. 1-June 24, 1923—Cases 313. Corresponding period, 1923, 1,039 cases.
India:				
Rangoon	June 15-21	19	16	
Indo-China:				
Saigon	May 18-31	5	1	Including 100 square kilometers of surrounding country.
Iraq:				
Bagdad	June 8-14	4	3	
Persia:				
Abadan	May 1-31	20	12	
Bander Abbas	do	11	6	
Bushire	do	1		Landed at quarantine.
Mohammerah	do	111	78	
Siam:				
Bangkok	June 8-14	1	1	

SMALLPOX.

Canada:				
Manitoba—				
Winnipeg	July 13-19	1		
Ontario—				
Sarnia	July 20-26	1		
China:				
Amoy	June 8-21			Present.
Chungking	June 15-21			Do.
Foochow	June 15-21			Do.
Manchuria—				
Harbin	June 17-23	1		
Nanking	June 15-28			Do.
France:				
Limoges	Apr. 1-30		1	
Haiti:				
Port au Prince	July 6-12	2		Developed at Cape Haitien.
India:				
Karachi	June 22-28	12	1	
Madras	June 22-28	7	2	
Rangoon	June 15-21	4	4	
Indo-China:				
Saigon	May 18-June 7	36	19	Including 100 sq. km. of surrounding country.
Jamaica				July 6-12, 1924: Cases, 7 (reported as alastrim).
Kingston	July 6-12	2		Reported as alastrim.
Java:				
East Java—				
Soerabaya	May 18-24	99	15	
West Java—				
Batavia	May 31-June 6	1		

[1] From medical officers of the Public Health Service, American consuls, and other sources.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued.

Reports Received During Week Ended August 8, 1924—Continued.

SMALLPOX—Continued.

Place.	Date.	Cases.	Deaths.	Remarks.
Latvia				May 1-31, 1924: One case.
Mexico:				
Mexico City	June 15-28	15		
Tampico	July 11-20	2	1	
Portugal:				
Oporto	June 22-28		6	
Do	June 29-July 12	2	2	
Siam:				
Bangkok	June 8-14		1	
Syria:				
Damascus	June 6-12	5		

TYPHUS FEVER.

Algeria:				
Algiers	June 1-30	5	1	
Chile:				
Iquique	June 22-28		1	
Valparaiso	June 15-21		2	
Do	June 29-July 5		3	
Egypt:				
Alexandria	June 25-July 1	1		
Esthonia				Apr. 1-May 31, 1924: Cases, 32.
Latvia				May 1-31, 1924: Cases, 43.
Mexico:				
Mexico City	June 15-28	15		Including municipalities in Federal District.
Turkey:				
Constantinople	June 15-21		1	

Reports Received from June 28 to August 1, 1924.[1]

CHOLERA.

Place	Date	Cases	Deaths	Remarks
India				Apr. 20-May 24, 1924: Cases, 45,434: deaths, 33,431.
Bombay	May 4-10	1		
Calcutta	May 11-June 7	137	116	
Madras	June 1-21	7	6	
Rangoon	May 11-June 14	65	49	
Indo-China:				
Saigon	Apr. 27-May 3	1	1	
Philippine Islands:				
Province—				
Cagayan	Mar. 30-Apr. 5	1	1	
Laguna	May 18-24	1	1	
Siam:				
Bangkok	May 4-June 7	14	12	

PLAGUE.

Argentina:				
Chaco Territory				Apr., 1924: Cases reported.
British East Africa:				
Kenya—				
Tanganyika Territory	Feb. 24-Mar. 1		1	
Canary Islands:				
Teneriffe—				
La Laguna	June 20	1		
Ceylon:				
Colombo	May 11-June 14	8	3	Ten plague rodents
Chile:				
Antofagasta	June 1-16	4		
China:				
Foochow	May 4-June 14		24	Cases not reported.

[1] From medical officers of the Public Health Service, American consuls, and other sources.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued.

Reports Received from June 28 to August 1, 1924—Continued.

PLAGUE—Continued.

Place.	Date.	Cases.	Deaths.	Remarks.
Ecuador:				
Eloy Alfaro	May 16-31	1		
Guayaquil	May 16-June 15	2		Rats taken, 14,987; found infected, 88.
Egypt				Jan. 1-June 26, 1924: Cases, 316.
City—				
Alexandria	Apr. 2	1	1	
Port Said	Apr. 24-June 3	2	1	
Suez	Jan. 2-June 26	11	5	
Province—				
Assiout	Apr. 1-June 18	40	31	
Beni-Suef	June 21	3	3	
Charkieh	Jan. 31	1	1	
Fayoum	Feb. 18-June 19	105	32	
Gharbia	Apr. 21-June 17	2	1	
Ghirga	Jan. 17-May 13	10	3	
Kalioubieh	Jan. 6-May 22	10	1	
Kena	Apr. 9-May 17	44	26	
Menoufieh	Jan. 2-June 12	48	31	
Minia	Feb. 5-June 26	39	20	
Greece:				
Patras	July 7	36		
India				Apr. 20-May 24, 1924: Cases, 74,793; deaths, 60,790.
Bombay	May 4-June 14	48	43	
Calcutta	May 11-June 14	10	10	
Karachi	May 18-June 21	16	13	
Madras Presidency	May 18-31	7	2	
Rangoon	May 11-June 14	48	49	
Indo-China:				
Saigon	May 4-10	1	1	Including 100 square kilometers of surrounding country.
Iraq:				
Bagdad	Apr. 20-June 7	114	56	
Japan:				
Shizuoka Prefecture—				
Higashi				To June 20, 1924: Cases, 2; death, 1.
Madagascar:				
Tananarive Province				Apr. 1-30, 1924: Cases, 105; deaths, 99.
Tananarive Town	Apr. 1-30	9	9	
Other localities	do	96	90	
Persia:				
Bushire	do	1	1	
Peru				May 1-31, 1924: Cases, 5; deaths, 5.
Lima (city)	May 1-31	3	4	
Lima (country)	do	1		
Mollendo	do	1	1	
Siam:				
Bangkok	May 4-10	2	2	
Union of South Africa				Apr. 27-June 7, 1924: Cases, 28; deaths, 14. Dec. 16, 1923, to May 31, 1924: Cases, 347; deaths, 208 (white, 51 cases, 26 deaths; native, 296 cases, 182 deaths).
Orange Free State				May 11-June 7, 1924: Cases, 18; deaths, 7.

SMALLPOX.

Bolivia:				
La Paz	May 1-31	2	4	
Brazil:				
Bahia	May 18-24	1		
Porto Alegre	May 18-June 14	1	1	
Rio de Janeiro	May 18-24	2		
British East Africa:				
Kenya—				
Mombasa	May 4-31	3		
British South Africa:				
Northern Rhodesia	May 6-June 9	57	1	Natives.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued.

Reports Received from June 28 to August 1, 1924—Continued.

SMALLPOX—Continued.

Place.	Date.	Cases.	Deaths.	Remarks.
Canada:				
British Columbia—				
Vancouver	June 15–28	11		
Do	June 29–July 12	13		Not including suburbs.
New Brunswick—				
Restigouche County	June 1–July 12	11		
Ontario				June 1–30, 1924: Cases, 24.
Windsor	June 22–28	1		
Quebec—				
Montreal	June 8–14	1		
Chile:				
Antofagasta	June 11	2		Under treatment at Lazaretto, 2 cases.
Valparaiso	June 1–7		1	This report covers the two principal districts of Valparaiso.
China:				
Amoy	May 11–June 7			Present.
Antung	June 9–22	34	3	
Chungking	May 11–June 14			Do.
Foochow	May 18–June 14			Do.
Hongkong	May 4–24	25	19	
Manchuria—				
Dairen	May 12–June 1	20	7	
Harbin	May 13–19	1		
Nanking	May 18–June 14			Do.
Shanghai	May 25–31		1	
Tientsin	May 4–June 14	10	1	British municipality.
Chosen:				
Fusan	May 1–31	1		
Denmark:				
Copenhagen	May 18–31	3	1	
Egypt:				
City—				
Alexandria	June 4–10	1		
Cairo	Feb. 19–Apr. 15	30	5	
Port Said	June 18–24	1	2	
France:				
Marseille	May 1–31		1	
Paris	May 21–31	2		
Great Britain:				
England and Wales				May 25–June 28, 1924: Cases, 342.
Counties—				
Derby	May 25–June 28	150		June 29–July 5, 1924: Cases, 62.
Do	June 29–July 5	20		
London	do	1		
Northumberland	May 25–June 28	61		
Do	June 29–July 5	7		
Nottingham	May 25–June 28	29		
Do	June 29–July 5	13		
Yorks (North Riding)	May 25–June 28	54		
Do	June 29–July 5	5		
Greece:				
Saloniki	Apr. 21–May 4	* 7	2	
India				Apr. 20–May 24, 1924: Cases, 17,069; deaths, 3,893.
Bombay	May 4–June 14	339	229	
Calcutta	May 11–June 14	15	15	
Karachi	May 18–June 21	39	17	
Madras	May 18–June 21	25	8	
Rangoon	May 11–June 14	48	15	
Indo-China:				
Saigon	Apr. 27–May 17	81	45	
Iraq:				
Bagdad	Apr. 20–May 24	8	1	
Italy:				
Messina	May 26–June 1	1		
Jamaica				June 1–28, 1924: Cases, 141. (Reported as alastrim.) June 29–July 5, 1924: Cases, 38.
Kingston	June 1–28	6		Reported as alastrim.
Do	June 29–July 5	4		
Japan:				
Kobe	May 26–June 21	3		
Nagoya	June 8–14	2		

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued.

Reports Received from June 28 to August 1, 1924—Continued.

SMALLPOX—Continued.

Place.	Date.	Cases.	Deaths.	Remarks.
Java:				
East Java—				
Soerabava	Apr. 13–May 17	170	59	
Madoera Residency—				
Sampang	May 22			Epidemic.
Latvia	Apr. 1–30	1		
Mexico:				
Guadalajara	May 1–June 30	9	4	
Do	July 8–14		1	
Mexico City	May 4–June 14	81		Including municipalities in Federal district.
Salina Cruz	May 25–31	1	1	
Tampico	June 14–20	2		
Do	July 1–10	4	4	
Palestine				June 17–23, 1924: 20 cases in northern district.
Samaria Province—				
Samak	May 27–June 2	1		
Poland				Mar. 30–May 3, 1924: Cases, 164 deaths, 7.
Portugal:				
Lisbon	May 25–June 21	7	1	
Do	June 29–July 5	2		
Oporto	May 11–June 21	18	10	
Russia				Jan. 1–Dec. 31, 1923: Cases, 44,628.
Siam:				
Bangkok	Apr. 27–May 17	3	4	
Spain:				
Barcelona	Year 1923	160		
Malaga	June 29–July 5		2	
Valencia	June 8–21	3		
Straits Settlements:				
Singapore	May 4–24	2	1	
Sumatra:				
Medan	Jan. 1–31	5		
Switzerland:				
Berne	May 25–June 28	22		
Syria:				
Damascus	May 28–June 3	7		
Tunis:				
Tunis	May 27–June 30	17	4	
Do	July 1–7	1	3	
Turkey:				
Constantinople	June 1–7	1		
Union of South Africa				Mar. 1–Apr. 30, 1924: Cases, 80 (white, 5; native, 75).
Cape Province	May 4–31			Outbreaks.
Orange Free State	May 4–10			Do.
Transvaal	May 4–31			Do.
On vessel:				
S. S. Karoa	May 7	1		At Durban, South Africa, from Bombay, India. Vessel left Bombay Apr. 16, 1924. Patient, European.
S. S. Mount Evans	July 8	1		At Key West, Fla., from Manchester, England.

TYPHUS FEVER

Algeria:				
Algiers	May 1–31	19	8	
Brazil:				
Porto Alegre	June 1–7		1	
Chile:				
Antofagasta				June 16, 1924: Two cases in Lazaretto.
Concepcion	May 20–26		3	
Talcahuano	May 25–31	2		
Valparaiso	May 25–June 14		9	
China:				
Antung	June 2–16	6		
Chungking	May 11–June 14			Present.
Chosen:				
Chemulpo	May 1–31	7		
Seoul	do	25	2	

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued.

Reports Received from June 28 to August 1, 1924—Continued.

TYPHUS FEVER—Continued.

Place.	Date.	Cases.	Deaths.	Remarks.
Egypt:				
Cairo	Feb. 19–Apr. 15	17	9	
Great Britain:				
Ireland—				
Dublin	June 8–14	1		
Greece:				
Saloniki	Apr. 20–May 4	6		
Iraq:				
Bagdad	Apr. 27–May 10	2		
Latvia	Apr. 1–30	39		
Mexico:				
Guadalajara	May 1–June 30	2	2	
Mexico City	May 4–June 7	44		Including municipalities in Federal district.
Palestine:				
Jaffa	June 17–23	1		
Poland				Mar. 30–May 3, 1924: Cases, 1,543; deaths, 142. Recurrent typhus: Cases, 27; deaths, 3.
Portugal:				
Oporto	June 15–21		1	
Russia				Jan. 1–Dec. 31, 1923: Cases, 242,890. Recurrent typhus: Cases, 258,271.
Syria:				
Aleppo	June 8–14	1		
Tunis:				
Tunis	May 27–June 9	4		
Turkey:				
Constantinople	May 18–June 7	7	1	
Union of South Africa				Mar. 1–Apr. 30, 1924: Cases, 257; deaths, 26 (white, cases, 18; deaths, 1; native, cases, 239; deaths, 25).
Cape Province	Mar. 1–Apr. 30	144	11	
Do				June 1–7: Outbreaks.
Natal				Mar. 1–Apr. 30, 1924: Cases, 9; deaths, 2.
Do				June 1–7: Outbreaks.
Durban	Apr. 20–26	1		
Orange Free State	Mar. 1–Apr. 30	55	8	
Do				June 1–7: Outbreaks.
Transvaal	do	31	4	
Johannesburg	May 11–24	2		

YELLOW FEVER.

Brazil:				
Pernambuco	May 11–17	2	1	

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